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A RADIOLOGICAL STUDY OF THE PLACENTAL STAGE OF LABOUR*

BY

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THE modern phase of interest in the third stage of labour can be regarded as dating back to Baudelocque (1793) who suggested that the placenta separates during the second stage of labour, a view which was later supported by Schultze (1867). The subsequent 150 years saw the Duncan (1871) and Schultze (1867) controversy over the method of separation of the placenta and also saw introduced the concept that it does not separate until 15 to 20 minutes after the birth of the baby—a concept on which practice was based during the first half of this century. There was, however, a third view sponsored by Werth, and Franz (1916, 1918), to the effect that, if the baby is born during a contraction, the placenta leaves the uterine wall as the trunk of the baby is expelled, whereas, if the baby is extruded by voluntary effort between the pains, separation may be delayed.

All manner of methods were used during the ensuing years in the attempt to determine which, if any, of these views as to the time and method of placental separation is correct. These included intra-uterine palpation immediately after the birth of the baby (Werth; Franz, 1916, 1918; Glöckner; Holzapfel; Leff, 1929; Graber, 1950); observations made at the time of Caesarean section (Ahlfeld; Keilmann and Voigt) and the Porro operation (Barbour, 1899); examination of women dying in labour, including a few cases in which frozen sections of the trunk were made (Barbour, 1899); tocography (von Györy and Domahidy, 1944); study of the placental transfer of substances such as chloroform initially (Zinstag), and radioactive isotopes more recently (Cox, 1950); and contrast-medium radiography (Warnekros, 1918; Weibel, 1919; Burton-Browne, 1949). As a result of such investigations and of the re-awakening of interest occasioned by the routine use of oxytocics at the end of the second stage of labour, there has in recent years been a return to the former view that the placenta separates quickly. There remains, however, some argument as to whether it separates late in the second stage or early in the third stage.

Radiography after injecting the cord with opaque material was first employed by Warnekros (1918) and Weibel (1919). Both were somewhat pre-occupied with the method rather than the time of separation, but Warnekros's well-illustrated paper is especially valuable in that in two of his cases he was able to visualize the placenta before, during and after the birth

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In an abbreviated form, it was presented at a meeting of the North of England Obstetrical and Gynaecological Society on the 18th February, 1955.

of the baby. Weibel's series was bigger but was limited to cases in which the cord was injected with radio-opaque material after the baby was born. He reached the conclusion that "in those cases where it was possible to say whether or not delivery of the foetus occurred during a pain, the immediate post-partum injection of the placental end of the umbilical vein showed that the placenta was already separated. In the other cases where the trunk was delivered by the mother's voluntary effort without the assistance of uterine contraction, the placenta was almost invariably found to be still attached."

Warnekros, besides confirming this statement of Weibel's, reported on two cases in which the cord was injected during the first or second stage of labour. In one, the opportunity to inject the placenta occurred when intranatal death of the foetus was associated with prolapse of the cord, and the other was a case of twins in which the placenta of the first twin was injected while the second baby was still undelivered. He concluded that in both cases the placenta required one or two third stage uterine contractions to complete its separation. Nevertheless, this conclusion does not appear to have a firm basis because, in the case of the twins, the first radiograph taken after the birth of the second baby showed that the placenta had already separated, while study of the illustrations of the other case suggests that the placenta may have been already separated at the time when the foetal buttocks were leaving the vagina.

Despite its attractiveness, the method used by Warnekros and Weibel does not appear to have been used again until 1949, when Burton-Browne reported on 13 cases in which the cord was injected immediately after the birth of the baby. The significance of the reproduced radiographs is not easy to assess, but the author herself concluded that the placenta separates during the third stage and not during the second stage of labour. The weakness of this technique is that the injection involves a delay of at least one minute after the baby is born and this is the crucial time for the study of the placenta. This disadvantage is emphasized by all those who have carried out intra-uterine palpation for they find that, no matter how quickly a hand is inserted into the uterus after the birth of the baby, the placenta is found to be already lying free in many cases.

To overcome this disadvantage we decided that it is necessary to render the placenta radio-opaque *before* the baby is delivered and this immediately raised the difficulty of doing so without danger to either the mother or the foetus. Various methods were considered in consultation with senior obstetricians, with radiologists and physicists. The points on which we required to be satisfied were:

(i) That the injection of the cord itself would not injure the foetus.
(ii) That the radio-opaque medium would be harmless to both mother and child if perchance it escaped into their circulation.
(iii) That the exposure to X-rays involved in screening and in serial photography would not be dangerous to either party.
(iv) That the procedures involved would not in any way prejudice the management of the delivery.

In this respect we were fortunate to have available a combined X-ray and delivery room as part of the labour suite and it was possible to ensure that one of us always concerned himself only with the delivery while the other managed the radiological investigation.

Having satisfied ourselves on these points it remained to ensure that each patient was informed of what was proposed and that she readily gave consent to it.

The initial investigation was carried out on lines similar to those used by Warnekros, that is, the prolapsed cord of a known anencephalic foetus was used for the injection. However, during 1½ years, only 4 cases of this kind became available, and in each one the foetus was small and delivery rapid. Nevertheless, in 3 of these we were able to see the placental shadows in all three stages of labour.

Our experience of these, which revealed the rapidity of placental separation, allowed us to proceed with the next stage of the investigation with confidence in its safety. This involved the study of labours in which a normal baby presented by the breech. Here, the cord is available for injection as soon as half the foetus is delivered; the placenta can then be seen

radiologically during the latter part of the second stage, and during the whole of the third stage of labour.

Material

The injected placenta was studied in 29 cases. These include 4 cases of anencephaly, 24 cases of breech delivery and 1 case in which the cord was injected *after* the second stage was complete.

Technique

At the appropriate stage of labour the patient was transferred from the ordinary labour bed to a modified X-ray table on which the remainder of the delivery was conducted.

I. The Radiographic Factors

These varied from case to case according to the general build of the patient. Average figures were 70 kilo-volts and 70 milli-ampere-seconds, using standard screens and a Potter-Bucky diaphragm. The numbers of radiographs taken varied from 4 to 12 per case. An overhead tube was used and the exposures were antero-posterior. In the early cases radiographs were taken at the time of natural pauses in the delivery or at times which the obstetrician thought might be informative. In these it was necessary to have another member of the staff making notes of timing. Later, the procedure was simplified in that the radiographer took photographs at 30-second intervals during the final phase of the second stage and for as much of the third stage as was considered necessary. In the last 3 cases of the series the sequence of events was watched on the fluorescent screen and this proved advantageous in timing postero-anterior exposure of the films.

II. Injection of the Cord

As soon as the cord became available it was injected with 70 per cent diodine. In the first few cases only 20 ml. of the medium was used but, as it was found that this amount could not be relied upon to give clear pictures, the amount was subsequently increased to 40 ml. It might be objected that the injection of as much as 40 ml. may disturb the physiology of the third stage of labour and there is no proof that it does not. Nevertheless, this amount is insignificant compared with that which is used in the Mojon-Gabastou method of treatment of retained placenta and it still remains doubtful whether this method does in fact assist placental separation. Also, in the last 10 cases we milked the cord towards the baby before the first clamp was applied. This probably resulted in the withdrawal of more blood than the volume of fluid subsequently injected and the results did not differ significantly from those obtained previously.

After the successful injection of the umbilical vein in the first few cases, the possible advantages of injecting an artery were considered. Such an injection, being an imitation of the natural direction of flow through the placenta, might be expected to give a better filling. It was attempted twice and was successful once—and that in a case of anencephaly. However, in the course of time, a number of unintentional arterial injections enabled us to assess the relative values of the two routes. With one possible exception, entry of the needle into the artery was not attended by any greater resistance to the injection than that normally encountered in the vein. This was to be expected since the artery is of sufficient calibre to take such a fluid medium and is not constricted by spasm until the foetus resorts to pulmonary respiration.

III. Management of the Third Stage

In this stage fundal pressure and massage were carefully avoided and the supra-pubic pressure test for placental separation was not applied. Oxytocics were not given until the placenta had been expelled. When the usual signs indicated that the placenta was lying in the lower segment and vagina, it was delivered by cord traction. Occasionally, when the signs were equivocal and according to the usual practice of the hospital in such circumstances, two fingers were inserted into the vagina to ascertain whether the placenta was within reach, which it always was.

IV. Cases of Breech Presentation

The delivery was according to the technique described by Cox (1950) and, as mentioned previously, was always conducted by one of us not concerned with the radiographs. In 11 cases no anaesthesia was given other than self-administered trichlorethylene. In the remainder pudendal nerve block was supplemented by

intravenous sodium thiopentone for delivery of the head and shoulders. As soon as the cord became accessible, it was pulled down and clamped. Seventy per cent diodone was injected on the maternal side of the clamp and a second clamp was applied to prevent leakage. The cord was then divided and delivery was completed in the usual way. The baby was delivered within 6 minutes of the application of the first clamp in all except one case (where the interval was 7 minutes). The after-coming head was invariably delivered with forceps.

V. Cases of Anencephaly

The malformation was diagnosed antenatally and labour occurred spontaneously in some cases and was induced in others. When labour was induced by rupture of the membranes, the Drew-Smythe catheter was used so that the drainage could be controlled and stopped while there was yet a moderate amount of liquor in the uterus. In this way it was hoped that premature partial separation of the placenta would be avoided. The umbilical cord was injected if it became available over the os or within the vagina during the first stage.

VI. Injection of the Cord after Normal Delivery

This was carried out once as a pilot experiment mainly for testing the radiographic technique and was then abandoned for reasons stated previously.

Interpretation of the Radiographs

The interpretation of the radiographs of the injected placenta *in utero* is not so easy as might be supposed and, judging from the limited literature on the subject, this has been the experience of others. It has to be realized that a continuous three-dimensional process is being assessed by an interrupted two-dimensional technique and this immediately calls for caution in interpretation. Again, it is probable that uterine contractions modify the radiological appearances of the placenta in a purely temporary and insignificant fashion. Finally, apparent changes in the utero-placental relationship as revealed in the radiographs may be the result of rotation of the uterus which is accepted as being a common accompaniment of contraction. The possible effect of this factor on the relations of the vessels to each other will be referred to later.

The soft tissue shadow of the uterus is usually seen easily and its outline is often well defined by gas in the surrounding bowel. When this is so, its relation to the injected placenta is readily established. The degree of placental filling varies considerably from case to case even though the conditions of injection are standardized. To some extent this is explained by the variable length of the cords but it also depends on whether the arterial or the venous (or both) systems are filled. If the injection is intra-arterial there is a greater likelihood of the small vessels being shown. This is illustrated in Fig. 14. In this case both arteries were unintentionally injected and a remarkably detailed picture of the placental vasculature was obtained. The placental circulation appears to be a very free one since in quite a number of cases the medium, no matter whether it was injected into vein or into artery, was seen returning along the other vessels of the cord soon after the initial injection, despite the fact that the clamp converted the cord and placenta into a closed system. It is not clear whether this rapid return is due to large vessel anastomoses or to complete circulation through a small area of the placenta but it is not necessarily associated with a richly detailed picture.

Even when only the large vessels are outlined, it is possible to recognize changes in the utero-placental relationship. In 23 out of the 29 cases of the series, the radiographs were sufficiently clear to allow of an assessment of the state of the placenta at the time of delivery of the last part of the baby, though, for reasons indicated later, only 22 of these were suitable for study of radiological details.

Early Signs of Separation

The only incontestable radiological evidence that the placenta has separated is its descent in relation to the soft tissue outline of the uterus and to the bones of the maternal spine and pelvis. There are, however, other signs which alone or in combination may be sufficient to indicate that separation is taking place before

mass movement of the placenta puts the issue beyond doubt.

(1) *Changes in the Relation of the Placental Shadow to the Soft Tissue Shadow of the Uterus*

A gross increase in the space between the peripheral vessels of the placenta and the soft tissue outline of the uterus leaves little doubt that at the particular point separation has already occurred (Figs. 3 and 4, Case I; Fig. 10, Case III; Fig. 13, Case IV). Smaller increases in this gap, however, can only be assessed after making allowance for possible thickening of the uterine wall by retraction. According to the findings of Danforth and his associates (1942) in monkeys, and of Barbour (1894) who studied frozen sections of women dying in the third stage of labour, this thickening is by no means constant or uniform through the whole uterus. It can also be modified temporarily by contraction and since, as already mentioned, contraction may produce uterine rotation, yet another variable may be introduced. Our conclusion with regard to this early sign of separation of the placenta is that it is only reliable when the placenta is seen "in profile", that is, in antero-posterior radiographs when it has a fundal, cornual or lateral insertion. It may be reliable in the case of an anterior or posterior insertion of the placenta when the relationship of the upper edge with the fundus undergoes a gross change (Fig. 4, Case I).

(2) *Descent of the Lower Border of the Placenta*

Descent of the lower edge of the placenta is easy to recognize and to measure in relation to the maternal bones but it must be viewed in the light of possible coincident collapse of the lower segment or descent of the uterus as a whole (Figs. 6, 7 and 8, Case II; Figs. 10 and 11, Case III; Figs. 12 and 13, Case IV). It is convincing when, as in Case I, the vessels of the lower edge are obviously resting on the after-coming head during breech delivery. If, at the same time as the lower edge descends, the lower main vascular trunks "fan out", or the conditions suggested in the next section are in evidence, the sign is probably equally reliable.

(3) *Changes in Relative Filling of Different Parts of the Placenta*

On comparing successive films from the same patient it is common to find that the medium undergoes re-distribution in such a way that the shadow of one part of the placenta (usually the upper) becomes rarefied while that of another part (usually the lower edge) becomes denser and more homogenous. At the same time, the cord may take on an appearance of greater turgor. This sign, when present, usually appears when the lower part of the placenta reaches the level of the upper part of the sacrum and care is necessary to distinguish the contribution made by the sacral shadow (Figs. 6, 7 and 8, Case II; Figs. 10 and 11, Case III). If this appearance is seen in one film only it is not significant because it could be produced by a uterine contraction wave.

(4) *Crowding of the Vessels*

It might be expected that the Schultze method of placental separation would produce crowding of the larger vessels so that the branches of the vascular tree would come to resemble those of the poplar rather than the oak. Reduction in the size of the placental site would also have the same effect. We have seen this sign but it requires even more cautious interpretation than the previous ones since a similar appearance can be caused by contraction and rotation of the uterus. It is only significant when it is progressive or when it is accompanied by other evidence of separation (Fig. 6, Case II). The possible error which can arise from uncritical acceptance of this sign is underlined by a study of the change in the appearance of the forceps blades caused by a minor degree of rotation (Fig. 7, Case II).

(5) *Divergence of Vessels*

An opposite change in the disposition of the vessels is sometimes seen. This widening of the gap between the vessels is usually present in the lower part of the placenta and coincides with crowding of the vessels elsewhere. The appearance suggests that the upper portion of the afterbirth is still attached and subjected to the compression effect of the upper segment, while the lower part is lying free below the retraction

ring and is able to "fan out". On the other hand, it might be explained merely by a contraction wave affecting the upper before the lower part of the uterus and it does not necessarily by itself indicate placental separation. Exceptionally, as in Fig. 3, Case I, the effect is seen in the upper part of the placenta while the lower part is relatively unchanged.

(6) *Changes in the Curvature of the Small Vessels*

Burton-Browne (1949) described changes in the curvature of the small vessels as evidence of placental separation but we were unable to find any significant alterations in this respect.

Late Signs of Separation

The most conclusive evidence of the separation of the placenta is its descent into the lower uterine segment and vagina. Except when the third stage is clearly abnormal this occurs remarkably quickly.

Changes in Uterine Shape

Study of the soft tissue outlines of the uterus emphasizes that retraction is a process which occurs in all planes, affecting the circumference, width and depth of the uterus as well as its length. At any one time, however, one part of the organ may be more affected than another, or one component be more obvious than others. Thus, at the end of the second stage, narrowing of the uterus is the dominant feature in some radiographs (Fig. 13, Case IV) while in others the uterus is shortened from above downwards while retaining a globular shape (Fig. 11, Case III; Fig. 8, Case II). The appearance of retraction mainly in one plane may persist until complete expulsion of the foetus and occasionally until the end of the third stage, but ultimately uniform retraction takes place and invariably results in a small, round uterine shadow.

There were 3 cases in which placental separation occurred before there was evidence of significant uterine retraction. In the remainder, retraction appeared to precede separation.

Analysis of the Findings

The analysis of the radiological findings in respect of placental separation is confined to 22 cases (20 of breech delivery, 2 of anencephaly). Of the total of 29 cases, 5 are deleted because the pictures are of poor quality, 1 because the third stage was disturbed by deep ether anaesthesia at the time of delivery, and 1 because the cord was not injected until after the birth of the baby.

Frequency of Radiological Signs of Placental Separation

(1) *Early Signs of Separation*

(*a*) Change in the depth of the uteroplacental space occurred to a significant degree in 9 cases.

(*b*) Descent of the lower edge sufficient to indicate its separation was seen in 16 cases.

(*c*) Changes in relative filling of the different parts of the placenta were present in 13 cases.

(*d*) Crowding of the vessels was seen in 11 cases.

(*e*) Widening of the angles between the vessels was seen in 7 cases.

(2) *Late Signs of Separation*

Descent of the placenta into the lower segment and vagina was apparent in the X-rays in 21 of the 22 cases before there had been any interference such as traction on the cord. In one of the 21 cases, however, despite clear clinical signs of descent, and minimal resistance during cord traction, a cotyledon was left lying above the retraction ring and had to be removed manually. Subsequent careful inspection of the X-rays in this case failed to show evidence of the retained cotyledon and it can only be concluded that the medium failed to penetrate it or that its shadow was lying over the maternal spine and could not be distinguished from the latter.

Condition of the Placenta at the Time of Expulsion of the Baby

The evidence of mass movement of the placenta or of disturbance of the *whole* uteroplacental relationship led us to conclude that, at the time of delivery of the last part of the baby, the placenta was totally separated in 9 of the 22 cases. In 6 of these cases it was judged to be already in the lower segment or the vagina.

FIG. 1

Case I. The umbilical vein and the vessels of the placenta are outlined. The uterine outline is emphasized by gas in the surrounding bowel. The head is about to enter the pelvic brim transversely.
(*First picture—immediately after injection.*)

FIG. 2

Case I. The lowest part of the placenta, relieved of the pressure of the foetal head, has now filled with dye. The vessels of this part are kinked, suggesting that it has already separated and is resting on the foetal head.
(*Second picture—$\frac{1}{2}$ minute after injection.*)

J.M., J.K.W.

FIG. 3

Case I. The vessels of the upper part of the placenta have become more widely separated and near the midline the distance between them and the fundus has increased. At the same time, the medium has undergone a partial redistribution so that the lower part of the placenta has increased in density at the expense of the upper part.
(*Fourth picture—1½ minutes after injection.*)

FIG. 4

Case I. Most of the placenta has now accompanied the head into the lower segment.
(*Sixth picture—2½ minutes after injection.*)

J.M., J.K.W.

FIG. 5

Case II. The cord is compressed by the foetal head which is negotiating the brim of the pelvis transversely.
(*First picture—immediately after injection.*)

FIG. 6

Case II. The main vessels have become crowded and a portion of placenta from the right side of the fundus has become detached and has fallen below the main mass. A change has occurred in the relative filling of the parts of the placenta; the density of its lower part is enhanced by the sacral shadow.
(*Third picture—1 minute after injection.*)

FIG. 7

Case II. The genuine nature of the relative filling change has become apparent. The lower edge of the placenta has descended from the level of S.1 to S.2.
(*Fifth picture—2 minutes after injection.*)

FIG. 8

Case II. The placenta is entering the lower part of the birth canal in "Duncan fashion".
(*Seventh picture—3 minutes after injection.*)

J.M., J.K.W.

FIG. 9

Case III. This shows good filling of the smaller vessels of a fundal placenta. The head is disposed transversely in its approach to the pelvic brim.
(*First picture—immediately after injection.*)

FIG. 10

Case III. Part of the placenta (from the left side of the fundus) has become detached and lies below the main mass, producing an almost homogeneous shadow over the first piece of the sacrum. The rotation of the head is now almost complete.
(*Eighth picture—3½ minutes after injection.*)

J.M., J.K.W.

FIG. 11

Case III. The lower edge of the placenta has descended still further and the redistribution of the dye is more obvious. The globular form of the uterus is retained despite considerable longitudinal retraction. There is an increase in the depth of the utero-placental space at the right cornu. These features along with the gross change in the relations of the large vessels to each other, suggest complete separation of the placenta.
(*Ninth picture—4 minutes after injection.*)

FIG. 12

Case IV. Gas in the surrouding bowel gives greater definition to the uterine outline and simplifies the interpretation of changes due to retraction and placental separation (compare with Fig. 13).
(*Second picture—$\frac{1}{2}$ minute after injection.*)

J.M., J.K.W.

FIG. 13

Case IV. This picture shows a gross increase in the depth of the utero-placental space on the right side of the uterus. Retraction has caused a narrowing of the uterine shadow without any coincident fall in the height of the fundus.

(*Second picture—3 minutes after injection.*)

FIG. 14

Accidental injection of both umbilical arteries has produced a richly detailed picture of the placental vasculature.

FIG. 16

Intra-uterine foetal cardio-angiogram produced by injecting towards the foetus rather than the placenta in a case of anencephaly.

FIG. 15

Maternal pyelogram observed 20 minutes after initial injection in a case of anencephaly.

J.M., J.K.W.

In a further 10 patients it was at least partially separated while in the other 3 it was apparently undisturbed. It should be noted, however, that these findings apply almost entirely to breech delivery, which is characterized by considerable uterine retraction before the foetal head is delivered. They are not necessarily applicable to cases of head presentation.

The Time Taken for Placental Descent into the Lower Birth Canal

In 3 of the 22 cases, the radiographs were not timed and all that can be said of these is that the placenta descended into the lower part of the birth canal quickly. In a further case manual removal of the placenta was necessary. In the remaining 18 cases spontaneous descent of the placenta into the lower segment or vagina was seen as follows:

At the time of completion of the second stage	6 cases
In less than 2 minutes after the end of the second stage	11 cases
In less than 3 minutes after the end of the second stage	15 cases
In less than 5 minutes after the end of the second stage	18 cases

In a number of cases the first radiographs obtained immediately after injection of the cord revealed evidence that placental separation had already commenced or taken place.

The "signs of separation" or the "signs of descent" are usually described as follows:

(*a*) The cord lengthens and a flow of blood comes from the vagina.
(*b*) The uterus becomes smaller, rounder and more mobile.
(*c*) The fundus rises in the abdomen.

Our radiographs permit comment on two of these clinical signs. That the uterus becomes a small round organ lying low in the abdomen is a constant finding. On the other hand, the movement of the fundus is an uninterrupted descent and *there is no evidence of elevation when the placenta enters the lower segment and vagina.*

Our observations show that, even with a technique which avoids the use of intravenous oxytocics, the placenta can often be delivered safely at a much earlier time than is generally recommended. Indeed they suggest that the placenta is nearly always ready for delivery within 5 minutes of the end of the second stage. The findings also indicate that the clinical signs of descent of the placenta quite frequently lag behind the physiological events. In several of our cases radiological study revealed that the placenta had already separated and *descended* at a time when the obstetrician was still waiting for the clinical signs to appear. On the other hand, they may be present when a small part of the placenta is still detained in the upper segment. The accepted clinical signs are therefore unreliable in practice, and this means that tests for separation such as suprapubic "dipping" and even a two-finger vaginal examination have an important place in the management of the third stage of labour.

The Relation of the Time of Separation to Birth During or Between Contractions

It was mentioned previously that earlier writers suggested that delivery of the foetus between contractions results in later separation and expulsion of the placenta. On this point we have no evidence to present, for in nearly all our cases delivery was of the assisted breech variety. It may be stated, however, that if this procedure is regarded as comparable to delivery between contractions, this circumstance does not appear to have retarded the process of placental separation.

The Effect of Anaesthesia on the Time of Separation

Only 1 patient in the whole series was delivered while deeply under the influence of ether anaesthesia and in that case manual separation and removal of the placenta was necessary. This may have been coincidental but it is in keeping with the traditional views about the effect of anaesthesia on the uterus. Manual removal of the placenta was necessary in only 1 of the remaining 28 patients who received trilene analgesia or thiopentone, and she had a unicornuate uterus.

There was no detectable difference between the third stages of thiopentone-treated cases and those in which only trichlorethylene was used. Here it should be noted that the thiopentone

was not administered until the time at which the cord was injected, that is, until placental separation had already commenced in some cases.

Influence of Uterine Form

Exception might be taken to deductions based on a series composed predominantly of breech deliveries on the ground that the process of placental separation and descent might be influenced by the abnormally high proportion of uterine malformations which is believed to occur in such cases. Such malformations, however, tend to delay rather than hasten the separation and delivery of the placenta. Hysterography was carried out 3 months after delivery in 14 of the 22 analyzed cases and in these the uterine forms were distributed as follows:

Normal	11
Subseptate	1
Unicornuate	2

The Mechanism of Placental Separation

Study of the radiographs allows comment on the old controversy regarding the Schultze and Duncan methods of placental separation. Among 21 cases in which the process could be assessed there was 1 in which separation appeared to occur centrally and peripherally at the same time. In 17 of the remaining 20 cases there was clear evidence of the Duncan method, separation commencing as a rule at the lower edge of the placenta. There were only 3 cases in which the placental separation commenced centrally (Schultze method).

Moreover, the old argument that the form taken by the placenta as it leaves the vulva does not indicate its method of separation is substantiated by this investigation. The placenta which separates by the Duncan mechanism can appear at the vulva in the form of an inverted umbrella. This may result from traction on the cord but can occur spontaneously. Similarly, a Schultze separation can be followed by a Duncan extrusion.

The observation that the lower edge of the placenta usually separates first is not new and was frequently made by those who made intrauterine palpations to investigate the third stage. The findings in this respect are also in accord with those of Danforth and his colleagues (1942) on monkeys.

Incidental Observations on Breech Delivery

Compression of the Cord

A striking finding was the clear demonstration of the correctness of the established view that the after-coming head compresses the cord at the pelvic brim (Figs. 2, 5 and 12). Among the 20 breech cases with satisfactory X-rays, this effect was seen in 13. Whether the pressure is sufficient to occlude the vessels is probably not of great importance because our investigations confirm what has long been recognized clinically, namely that the baby at this stage can withstand complete interruption of its oxygen supply until the delivery of its mouth enables pulmonary respiration to become established.

Rotation of the Head

Only rarely in the present series was the head disposed other than transversely at the time when it was passing through the pelvic brim, though rotation occurred quite quickly once this plane had been passed (Figs. 1 and 2; 5 and 6; 9 and 10; 12). This finding supports the present day teaching that, during breech delivery, the foetal back should not be rotated to the front until the head has passed the pelvic brim, nor should forceps be applied until the head is low in the pelvic cavity and its rotation completed.

Comments on the Method of Investigation and Its Results

The method of investigation described here is one which can only be applied when expert assistance and special equipment (e.g., an X-ray room as part of the delivery suite) are available, and the care which was taken to make it safe proved justified. Thus, our expectation that the radio-opaque material might break through the placental barrier and enter the maternal circulation was realized in two cases of anencephaly. In one, it must have occurred almost immediately because a maternal pyelogram developed progressively from the first radiograph onwards (Fig. 15). In the second, there would appear to have been a slow absorp-

tion from the placenta and this resulted in the appearance of a cystogram and an amniogram in radiographs taken some hours later. These happenings emphasize the need to use a radiographic medium which is known to be harmless in the blood stream. A barium cream as used by Warnekros might have catastrophic results.

One of the technical difficulties is to ensure that the injection is made towards the placenta rather than towards the foetus. This does not arise in cases of breech delivery when the foetal connexion is seen and protected by a clamp. In the case of prolapsed cord associated with foetal malformation, however, it is extraordinarily difficult, and may be impossible, to decide which end of the loop connects with the foetus and which with the placenta. An error was made in one of the cases of anencephaly and the result was an intra-uterine cardioangiogram in which, in the original film, it is possible to identify all the main vessels throughout the body, including the ductus arteriosus (Fig. 16).

It remains to be stated that all 4 anencephalic foetuses were of course stillborn. Two other babies which presented by the breech suffered from hydrocephaly which had been diagnosed before labour: one was stillborn and the other died in the neonatal period.

One normal baby which presented by the breech was stillborn and the post-mortem examination showed no signs of injury. Its loss was attributed to asphyxia although the delivery was not attended by any unusual difficulty and only occupied 4½ minutes from the time the trunk was born as far as the umbilicus. The radiography did not appear to play any part in its death which is to be regarded as one of the hazards ever present with breech delivery.

The conclusions drawn from this investigation are in many respects tentative because of the small number of cases and because of the difficulty arising from the fact that only lateral, fundal and cornual placentas are adequately seen in the antero-posterior radiographs employed. In fact, most placentas are situated on the anterior and posterior walls of the uterus (Whitehead, 1953) and would require lateral radiography in order to represent them adequately and this is technically difficult and might interfere with the delivery, especially when the breech presents. Cornual and fundal implantations are, however, relatively common with persistent breech presentations so such cases are more favourable for antero-posterior radiography.

It must also be emphasized that the findings apply mainly to breech deliveries in which there is an interval between the complete evacuation of the upper segment and the birth of the last foetal part, an interval which may be as long as 5 to 6 minutes even though it is usually shorter. In so far as the physiology of the placental separation is concerned, therefore, it may be said that in breech labour the effective third stage commences before complete delivery of the infant because the uterus has considerable opportunity for retraction before the foetal head escapes from the pelvic cavity. In the case of head presentations, however, this opportunity arises almost simultaneously with the expulsion of the child.

Summary

(1) The historical aspect of interest in the third stage of labour is briefly reviewed.

(2) Previous reports of "cord injection placentography" are mentioned and the disadvantages of employing this or any other method of investigation after the birth of the baby are emphasized.

(3) Techniques are described for cord injection placentography with the foetus still undelivered in cases of anencephaly and breech delivery.

(4) A description is given of the radiological signs of early separation of the placenta, as revealed by this method.

(5) From the 29 cases investigated, 22 with complete data are analyzed and among them the frequency of the observed signs and the times of separation and descent are assessed.

(6) The findings show that the accepted clinical signs of placental separation and descent are unreliable.

(7) The placenta always separated and descended into the vagina within 5 minutes of the end of the second stage except when the third stage was pathological. In the majority of cases it descended even more quickly, often

before the after-coming head was extracted. Rapid separation and descent of the placenta was also noted when anencephalic foetuses were born head first.

(8) Incidental observations include the demonstration that the after-coming head almost always engages in the transverse diameter and only rotates after it has entered the pelvic cavity.

We wish to record our indebtedness to Mr. W. Jennings (Superintendent Radiographer) and his staff, who co-operated enthusiastically in this research. Our gratitude is also due to the staff of the Labour Ward for their willing and skilful assistance throughout.

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A PSYCHOLOGICAL INVESTIGATION OF PRIMIGRAVIDAE

I—Methods

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THIS investigation formed part of a socio-medical enquiry into first maternities in Aberdeen, and may be introduced by the following quotation:

"Efficient child-bearing will be influenced by many factors, but none so much as the mother herself. The mother is the product of heredity and environment, and therefore so far as possible the whole woman should be studied. We wish to know about her standard of education and that of her husband, and all that goes to make up her living conditions. We wish to know . . . what she thinks about childbirth and the rearing of children. We can then study how she behaves during pregnancy, labour, and lactation . . . In this way we may be able to build up a picture of various types and discover what psychological, social and physical influences affect reproductive performance and how they act" (Baird, 1949).

The study of "the whole woman" came to involve co-ordinated clinical, sociological, psychological and nutritional investigations of a large sample of patients. Since no similarly comprehensive enquiries have been reported a brief account of our methods may be useful and this paper deals with the technique of the psychological survey.

The difficulties, in work of this kind, are considerable. Few general conclusions can be drawn unless data are derived from a fairly large representative sample of patients; and whilst it may not be easy to obtain adequate co-operation from patients chosen at random, a sample composed of volunteers cannot be regarded as representative. Many psychological observations and measurements are difficult to interpret and few are wholly objective. Retrospective investigation of obstetrical abnormalities is seldom desirable, since neither patient nor psychologist is likely to be uninfluenced by knowledge of the outcome of pregnancy; on the other hand, a random sample investigated during pregnancy will include relatively few patients who subsequently develop severe morbidity. Some sociological and clinical aspects of the enquiry have been described elsewhere (Baird and Illsley, 1953; Thompson, 1954; Baird, 1952).

THE POPULATION STUDIED: SAMPLING AND ITS RESULTS

It was decided to investigate married primigravidae resident in Aberdeen; these form the largest and most important parity group. They are also the easiest to study; in Aberdeen, nearly 90 per cent of married primigravidae book for hospital confinement and the remaining 10 per cent for confinement in a private nursing home or in their own homes. It did not prove feasible to include the latter in the psychological investigation, which was therefore restricted to hospital booked married city primigravidae (B.M.C.P.). These attended a central antenatal clinic staffed by obstetricians from the hospital and medical and nursing

personnel from the city Health and Welfare Department. The extent to which hospital patients may be regarded as representative of all city primigravidae has been discussed by Baird and Thomson (1954).

The sample of B.M.C.P. was selected at booking. All primigravidae were listed and their social class determined; every sixth married patient giving an Aberdeen address was selected at the time of booking for special study. Shortly after the start of the survey, extra patients from the professional and managerial groups (Social Classes I and II), and from the semi- and unskilled working classes (Classes IV and V) were selected from cases remaining after taking out the 1-in-6 (random) sample. Some of those selected aborted or left the city before delivery, but similar losses were incurred by the population as a whole, so that both the sample and the population it represented could be defined in terms of patients *delivered* in the hospital. Losses due to other causes affected the sample only and were thus liable to bias the results of the survey.

Table I shows the number of B.M.C.P. in the samples, and the losses due to causes other than abortion or leaving the city. Complete psychological data were obtained from 278 out of the 332 cases in the sample, i.e., 84 per cent, and the success rate fell slightly with social class. Comparison with B.M.C.P. in general showed that the random and the three social class samples did not differ significantly from expectation in respect of age and height distributions, nor in respect of the incidence of forceps and operative delivery. On the other hand, the incidence of prematurity (birth weight under 5½ pounds) and of pre-nuptial conception was lower than expected, especially in the sample from Social Classes IV and V, due to the relatively heavy losses of patients at the lower end of the social scale, and of those whose "dates" were seriously in error. Again, those who booked after the 28th week of pregnancy had been excluded.

Survey Organization and Procedure

All patients were interviewed during the 6th month of pregnancy. Earlier interviews would have meant missing many "late bookers", and patients who were still working would have found it difficult to attend; losses due to premature labour and complications of pregnancy would have been frequent if the interviews had been arranged later than the end of the 6th month. The receptionist at the antenatal clinic was asked to tell the selected patients during a

TABLE I
Distribution by Social Class of Samples and of Patients Actually Studied

	Husband's Social Class	Random (1-in-6) Sample of all B.M.C.P.				Extra Samples	
		I and II	III	IV and V	All Classes	I and II	IV and V
A.	Cases sampled (*a*)	30	223	79	332	22	102
B.	Losses:						
	Late booking (*b*)	2	14	3	19	2	9
	Illness or "prematurity" (*c*) ..	—	4	5	9	—	2
	Excluded by psychologist (*d*) ..	—	5	1	6	—	2
	Refused co-operation	—	2	2	4	1	1
	Incomplete co-operation	—	12	4	16	2	9
C.	Complete data obtained (A–B) ..	28	186	64	278	17	79
	Per cent of A	93·3	83·4	81·0	83·6	77·3	77·5

NOTES: (*a*) Less 35 cases lost after sampling through abortion and leaving the city before delivery.
(*b*) Patients booked after normal time of interview (24th–28th weeks of pregnancy).
(*c*) Patients not interviewed owing to illness, or delivered before completion of interviews. In the latter, the degree of prematurity was less than would be expected from the stated date of the last menstrual period. In some cases the menstrual date was highly uncertain.
(*d*) Excluded on grounds of deafness, foreign nationality with language difficulty, etc.

routine visit that "Miss Scott would like to see patients who are expecting their first babies", and to make an appointment for the purpose. Nearly all patients accepted this as part of the normal clinic routine. The psychologist's office was on the clinic premises.

At the start of the interview, the psychologist asked the patient to co-operate in an investigation, sponsored by the Professor of Obstetrics, concerned with the problems of why some women had a more difficult time during pregnancy and labour than others. In return, they would be given an opportunity to ask questions about pregnancy and labour. The psychologist had attended numerous antenatal outpatient clinics and ward rounds in hospital, and observed and spoke to some 50 women during labour. She had thus obtained a clearer understanding of obstetric practice and was able to answer most questions asked by patients without further referral. Appointments were timed, so far as possible, to suit the patient's convenience, and it was found difficult to interview more than 4 patients a day. It is not always easy to maintain the interest of patients who have no personal reason to co-operate, and interviews were limited, in the light of experience, to two sessions of one hour each.

The first session was devoted to intelligence testing and to obtaining a short personal history, and the second to a study of personality by test and interview.

The first consisted of (*a*) Explanation of the reason for the enquiry, as already described (5 minutes). (*b*) Personal history (10–15 minutes). This covered the patient's health before and during pregnancy; education; employment; family background; husband's age, occupation and health; interests and hobbies of husband and wife. (*c*) Intelligence tests (40–45 minutes). These consisted of Raven's (1938) progressive matrices in the 20-minute version (a non-verbal test) and the Wechsler-Bellevue (verbal) intelligence scale. In the latter, 4 out of the 6 available sub-tests were used, namely, General Comprehension, Digit Span, Similarities, and Vocabulary (Wechsler, 1944).

The second session consisted of (*a*) Test of "neuroticism" (10 minutes). The Maudsley Medical Questionnaire (M.M.Q.) was used. (*b*) General interview (45–50 minutes). The interview covered the following topics: (*a*) knowledge of pregnancy, childbirth and child care; (*b*) attitudes towards pregnancy, labour, breast feeding and family planning; (*c*) attitudes towards husband, marriage and domesticity; and (*d*) mental health and general personal adjustment. Matters raised spontaneously by the patient herself were discussed first; these often included topics in the interview form (see Appendix). A set order of introduction was avoided, but questions dealing with attitude to husband, sex relations, views on and experience of birth control, and so on, were usually broached towards the end of the interview. To minimize error, all questions capable of a simple answer of the "Yes" and "No" type were marked thus on the interview form at the time. Detailed responses were noted verbatim whenever this could be done without interrupting the conversation; otherwise detail was filled in immediately the interview finished.

Grading of Test Scores. In order to allow comparisons between the results obtained by different tests it is usual to classify scores in relation to norms derived from an unselected reference population.

(a) *Raven's Progressive Matrices.* The scores obtained by patients in the random sample were grouped on a 5-point scale in accordance with service (Royal Naval) norms, the distributions obtained being shown in Table II. Service norms are the only ones so far available

TABLE II

Grades Used with Progressive Matrices Scores, according to Royal Navy Norms (Vernon and Parry, 1949)

Intelligence Grade		P.M. Scores	Normal Distribution Per cent. (R.N.)	B.M.C.P. Random (1-in-6) Sample	
				No.	Per cent.
A, B	Over average	45–60, 38–44	10, 20	41, 73	14·7, 26·3
C	Average	27–37	40	102	36·7
D, E	Below average	18–26, 0–17	20, 10	54, 8	19·4, 2·9
			100	278	100·0

for the timed version of this test. In the random sample, considerably larger numbers are in the A and B (over-average) grades than expected. Since similar skewness has been noted by other investigators using these norms (cf. Vernon and Parry, 1949), it would appear that the reference population was unrepresentative rather than that our sample of primigravidae contained an unusually high proportion of persons of over-average intelligence. It was, however, decided to retain the norms as a basis for grading scores obtained from the test.

(b) *Wechsler-Bellevue Verbal Scale.* The test was scored according to the procedure described by Wechsler (1944).* The scores are usually converted into intelligence quotients (I.Q.), which make allowance for the patient's age, since the ability to do most intelligence tests tends to decline slowly after age 25. Table III gives the distribution of I.Q.'s obtained in the random sample of B.M.C.P. in comparison with Wechsler's norms which were derived from an American reference population. There are two difficulties about using the grades in Table III. First, since I.Q. grades include a correction for age, this complicates all analyses in which it is desired to use age as an independent variable. Second, our data show a considerable excess of "below average" individuals on the norms used. This conflicts with the findings from the non-verbal test, and does not seem very plausible in fact. It was felt that no useful purpose would be served by retaining Wechsler's norms, and the total adjusted scores were graded directly, as shown in Table IV, to give an approximately normal distribution. Grades A and B signify the best 30 per cent and grades D and E the worst 30 per cent of the random sample of B.M.C.P.

(c) *Maudsley Medical Questionnaire.* This consists of 40 questions on neurotic symptoms or traits capable of being answered "Yes" or "No". Neurotically-disposed persons tend to give a higher number of "Yes" responses, i.e., obtain higher scores (Eysenck, 1952). For purposes of analysis, we grouped the scores obtained from the random sample into 3 groups, as follows:

Score	No. of Patients	Per cent
0–5 ..	61	22·1
6–12 ..	133	48·1
13 and over	82	29·7
	276*	100·0

* 2 patients were not tested.

TABLE III

Distribution of I.Q.'s on Wechsler-Bellevue Verbal Scale according to Wechsler's Norms

Intelligence Grade		I.Q.	Normal Distribution Per cent (Wechsler)	B.M.C.P. Random (1-in-6) Sample	
				No.	Per cent
A, B	Over average	120+	8·9	9	3·2
		111–119	16·1	35	12·6
C	Average	91–110	50·0	119	42·8
D, E	Below average	80–90	16·1	92	33·1
		–79	8·9	23	8·3
			100·0	278	100·0

TABLE IV

Distribution of Wechsler-Bellevue Weighted Scores Used in this Investigation

Intelligence Grade		Weighted Scores	B.M.C.P. Random (1-in-6) Sample	
			No.	Per cent
A, B	Over average	58+	26	9·3
		47–57	55	19·8
C	Average	37–46	115	41·4
D, E	Below average	31–36	54	19·4
		–30	28	10·1
			278	100·0

(d) *Stability Grading.* This was made immediately after the interview, and took into account the information on the mental health section of

* The score obtained on each sub-test is first converted to the same scale by weighting, and the total weighted score is then adjusted to correspond to that of the normal 5-sub-test version of the test.

the interview form (Appendix, Section 2, questions 8–14); it was also influenced by the patient's employment record, her reasons for leaving jobs, her past and present illnesses and emotional disturbances, her family and other personal relationships, and her manner and behaviour during interview. In the random sample, 14 per cent of patients were considered to be stable and well-adjusted (grade A), and 38 per cent to be unstable and poorly adjusted (grade C); 48 per cent were intermediate (grade B).

Discussion

In a survey of this kind, the choice of method depends on the aims of the study and on the degree of co-operation which can reasonably be expected from subjects.

Our basic aim was to obtain knowledge of the intelligence and personality of representative primigravidae, with a view to relating these characteristics to their social and clinical behaviour. The sample had to be large enough to permit statistical analysis, and the method of enquiry had to be such that the advantages of random sampling would not be jeopardized by a high failure rate.

In forming hypotheses, there was so much room for speculation that we were anxious to avoid canalizing the enquiry into a narrow channel, e.g., the relationship between emotional "tension" and behaviour during labour; on the other hand, it was not easy to define the aims of the enquiry in broad yet sufficiently exact terms. This made it difficult to decide what tests and other procedures to use. Many tests of ability seemed too specific for our purposes, while some less specialized tests would be difficult to put into practice. Difficulties with tests of personality were even greater (see below). Data from interview may be inaccurate and are often difficult to interpret.

Intelligence was thought likely to be related to those aspects of maternal behaviour which show social differentiation, e.g., family planning and use of social and medical services. There is a wide selection of tests dealing with intelligence, educational attainment, speed of reaction in various circumstances and so on, and we used two intelligence tests, one verbal and one non-verbal. The former is generally thought to be more closely related to environment and experience than the latter. Broadly speaking, the non-verbal test (Raven, 1938) measures general reasoning ability, while the four sub-tests of the Wechsler-Bellevue verbal scale measure, respectively, common-sense, memory and attention, logical thinking, and knowledge of the meaning of words. A consideration which influenced the choice of tests is that patients showed dislike of tests reminiscent of school, e.g., those involving mental arithmetic and "general knowledge".

Personality. It is easier to test attainment or aptitude than cheerfulness, tension, neuroticism, moodiness and so on. The length and complexity of most standard personality tests meant that the hour available would not be sufficient unless devoted entirely to one test. The Rorschach (ink-blot) and Thematic Apperception tests were tried in a pilot study but were disliked by patients who did not readily appreciate their relevance in relation to pregnancy. The Maudsley Medical Questionnaire is short and easy to administer, and its efficacy as a screening device for neurotic disposition has been shown (Crown, 1949). The stability grade and the M.M.Q. test score together supply assessments of personality adjustment, and can to some extent be used as a check on each other. Emotional adjustment may be related to some of the clinical phenomena of maternity.

The data obtained at interview depend entirely upon statements made by the patient, many of which are difficult to check, and assessments made from them are necessarily subjective. These defects and difficulties can be reduced by careful planning of the interview procedure, by verbatim recording of responses, and by grading responses according to a defined procedure and by cross-checking when possible. Whatever their defects, interview data are useful in interpreting the results of tests.

Summary

The methods used in an investigation of intelligence and personality in married primigravidae (booked hospital patients) are described. Of 332 patients randomly selected, 278 (84 per cent) co-operated in full. Co-operation was also obtained from 96 patients

from the "upper" and "lower" social groups. The reasons for losses are shown.

Patients attended two sessions of one hour each during the 6th month of pregnancy. Two standard tests of intelligence and one of "neuroticism" were applied, and an interview was designed to cover personal history, knowledge of maternity and adjustment to marriage and pregnancy. The methods of scoring and assessing the data are described and discussed.

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Appendix

Condensation of forms used for interview
(In the original forms there was space for recording responses verbatim and for additional notes)

Knowledge of Maternity

1. Did you attend the talks on insurance, diet or pregnancy?	YES	NO	?	
2. Have you read any books on pregnancy and/or labour?	YES	NO		
Which?.....				
3. Have you had a chance to discuss pregnancy or labour with anyone?	YES	NO	?	
With whom?.....	FULLY	PARTLY		
4. Have you heard about the Labour Talk?	YES	NO	?	
Will you manage to go to it?	YES	NO	?	
5. Have you ever visited the Maternity Hospital?	YES	NO		
What do you think / have you heard about it?	GOOD	AVERAGE	BAD	
Why are you going to hospital?.....				
6. Have you ever looked after children?	YES	NO		
Relationship..... Age.....	FULLY	PARTLY		
7. How many of a family are you going to have?	1 2 3 4 more			
Sexes.....	First—BOY	GIRL		
8. How long would you like between 1st and 2nd babies?	1 2 3 4 more years			
9. Have you heard of the Birth Control Clinic?	YES	NO	?	
Will you come for advice?	YES	NO	?	
10. Have you used any form of Birth Control?	YES	NO	?	
	H. Mech.	W. Chem.	Nat.	
At the time of conception?	YES	NO		
11. How did your mother get on having her family?	WELL	BADLY	?	
12. How did you feel about labour?	CALM	AFRAID	OTHER	
What do you feel about feeding the baby?	AF	BF		
	+	−	?	

APPENDIX—*Continued*

ADJUSTMENT TO MARRIAGE AND PREGNANCY

1. Did you plan to have your baby now?	YES	NO	?
2. What does your husband feel about the baby?			
3. Do you like cooking?	V. much	Yes	Not much
Do you like housework?	V. much	Yes	Not much
4. Does your husband help in the house?	Not at all		
	Occasionally		
	Always		
5. Do you think he'll give you a hand with the baby?	YES	NO	?
6. What kind of a person is your husband?	Calm	Excitable	
	Cheerful	Shy	
	Depressed		
	Irritable		
7. Do you manage all right on your money?	V. Good		
	Good		
	Fair		
	Difficult		
	Poor		
8. Do you usually sleep well?	YES	NO	?
Since pregnancy?	YES	NO	?
9. Do you usually dream much?	YES	NO	?
Since pregnancy?	YES	NO	?
10. Do you usually have any bother with your nerves?	YES	NO	?
Since pregnancy?	YES	NO	?
11. What sort of a person are you?	Calm		
Any change since pregnancy?	Excitable		
	Irritable		
	Shy		
	Easily upset		
	Depressed		
12. What medicines do you take?	Laxatives		
	Aspirins		
	Stomach powders		
	Other		
13. Do you usually have dizzy or fainting turns?	YES	NO	?
Since pregnancy?	YES	NO	?
14. Do you usually worry much over things?	YES	NO	?
Since pregnancy?	YES	NO	?

A PSYCHOLOGICAL INVESTIGATION OF PRIMIGRAVIDAE

II—Maternal Social Class, Age, Physique and Intelligence

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THAT the poorer social classes experience relatively high stillbirth and infant mortality rates has been known for many decades, and many investigators have used national and local statistics in attempts to find out what aspects of inferior social status are specially important. Social gradients in maternal and infant morbidity have been studied less extensively, but several enquiries—for example, those of Douglas (1950), Martin (1954) and Spence *et al.* (1954)—have shown that they exist. Investigations in Aberdeen have emphasized that social differences arise from a complex interaction of environmental and biological factors. It is usually difficult to show which are of primary importance but the overall picture is simple: in generally favourable conditions—good food, housing, education and so on—women usually grow well and are in good general health and, other things being equal, are less liable than average to, for example, contracted pelvis, stillbirth, prematurity and breast-feeding failure (Baird, 1947, 1949, 1952b, 1953; Baird and Illsley, 1953; Bernard, 1952; Hytten and Thomson, 1955). On the other hand, women reared in good social circumstances often postpone marriage and childbearing for a few years in the interests of education and economic security; in this respect they are at a disadvantage, being less fertile and more liable to difficult labour and inadequate lactation (Taylor, 1952; Baird, 1952a; Hytten, 1954).

Intelligence, like physical health, presumably has importance in relation to maternal behaviour and well-being. Intelligence test scores tend to be lower in the lower social groups than in the upper, in adults (Burt, 1943; Cattell, 1934; Himmelweit and Whitfield, 1944; Terman and Merrill, 1937) as well as in children (Scottish Council for Research in Education, 1953). Inferior intelligence, being related to inferior social status, is therefore likely to be associated with unfavourable mortality and morbidity rates. It is therefore of interest to determine trends of intelligence in relation to other possible influences on the course and outcome of maternity.

In this investigation we have studied some relationships between the intelligence test scores obtained by Aberdeen married primigravidae booked for hospital delivery, and their social class, age, height, and general physique and health. The relation of social status and intelligence to maternal behaviour will be described in a further paper.

The sample of patients studied and the intelligence tests used have been described in Part I of this series (Scott and Thomson, 1956). A verbal intelligence test (the Wechsler-Bellevue) and a non-verbal test (Raven's Progressive Matrices) were used. Social Class is based on the husband's occupation according to the method used by the Registrar General (General Register Office, 1951).

Results

Social Class. Table I shows the distribution of the patients in the random and in the three social class samples, according to the grades obtained on each intelligence test. As expected, more patients in Social Classes I and II obtained AB (over-average) gradings on the Wechsler-Bellevue test (73 per cent compared with 27 per cent in Social Class III, and 18 per cent in Social Classes IV and V). Conversely the percentages obtaining DE (under-average) gradings rose from 4 per cent in Classes I and II to 48 per cent in Classes IV and V. Similar trends exist between social class and Progressive Matrices grades but are less marked, possibly due to the lesser effect of environment and experience on non-verbal ability (Nisbet, 1953; Scott and Nisbet, 1954).

Table I includes the correlation coefficients between the two intelligence test scores; as expected, these are positive to a highly significant extent. The correlations increase as social status rises; though this trend is not statistically significant, it may reflect a lessening discrepancy between verbal and non-verbal abilities as average educational attainment increases.

Figure 1 shows the distribution of Wechsler-Bellevue grades by social class of the patient before and after marriage. The results of the non-verbal test give a similar but less smooth gradient. It is evident that a greater proportion of women who move up the social scale at marriage are in high intelligence test grades than of those who remain in the same class, and these in turn tend to be more intelligent than those who move down the social scale on marriage.

This result is not unexpected as Baird and Illsley (1953) and Illsley (1955) have shown that similar relationships exist between change of class at marriage and size of family of upbringing, the woman's occupation before marriage and

TABLE I
Distribution of Intelligence Test Grades in the Random and Social Class Samples

P.M. Grades		AB	C	DE	All	AB	C	DE	All
W.B. Grades		Numbers				Percentages†			
Random Sample (·61)*	AB	64	17	—	81	23	6	—	29
	C	40	50	25	115	14	18	9	41
	DE	10	35	37	82	4	13	13	30
	All	114	102	62	278	41	37	22	100
Social Classes I and II (·72)*	AB	31	2	—	33	69	4	—	73
	C	5	5	—	10	11	11	—	22
	DE	—	1	1	2	—	2	2	4
	All	36	8	1	45	80	18	2	100
Social Class III (·56)*	AB	40	11	—	51	21	6	—	27
	C	29	37	19	85	16	20	10	46
	DE	9	18	23	50	5	10	12	27
	All	78	66	42	186	42	36	23	100
Social Classes IV and V (·49)*	AB	18	7	1	26	13	5	1	18
	C	13	22	13	48	9	15	9	34
	DE	6	32	31	69	4	22	22	48
	All	37	61	45	143	26	43	32	100

* Numbers in brackets are correlation co-efficients between the scores of the two intelligence tests. All are "highly significant".

† Discrepancies in cross-totals of percentages are due to "rounding-off".

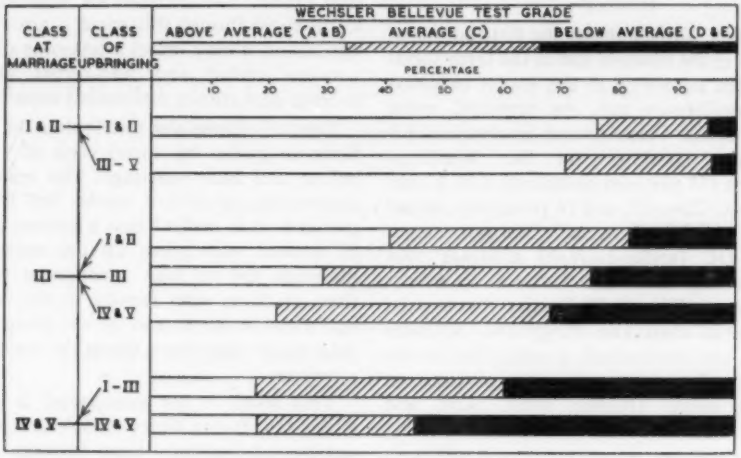
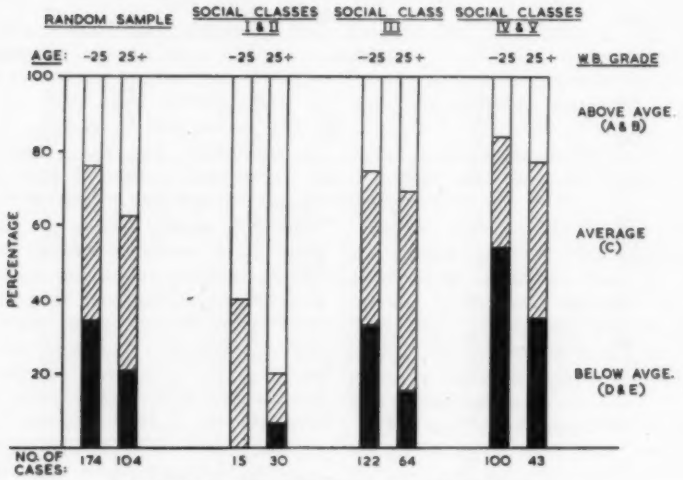


FIG. 1

Relationship of Wechsler-Bellevue intelligence test grades to inter-class movement at marriage.



Correlation between maternal age and test score:

·21*** ·12 ·22** ·18*

(Levels of significance: * 5 per cent; ** 1 per cent; *** 0·1 per cent)

FIG. 2

Distribution of Wechsler-Bellevue test grades by Husband's Social Class and Maternal Age.

her educational level—all factors associated with intelligence test scores. They have also shown that women who rise in social class at marriage tend to be superior in health and physique and to have a comparatively low incidence of pre-nuptial conception, and of prematurity, stillbirth and neonatal death.

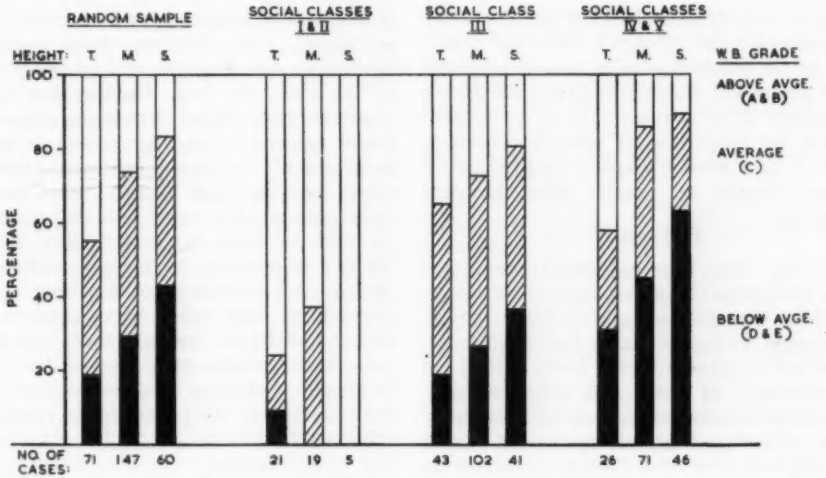
Age. National statistics show that women in the upper social classes are usually older at the time of the first delivery than those in the lower classes. Figure 2 shows the relationship between Wechsler-Bellevue intelligence grades and maternal age. Older women tend to obtain higher scores; as is confirmed by the correlation coefficients shown below the figure. This trend is not shown by the Matrices test scores, where correlation coefficients approximate to zero.

Height. Baird (1952b) and Baird and Illsley (1953) have shown that the proportion of tall primigravidae declines with social class. Figure 3 shows the relationship between Wechsler-Bellevue intelligence grades and maternal height, and indicates that tall women tend to obtain higher grades than small and *vice versa.* Within social classes, correlations increase as class declines, though not to a statistically significant extent.

Taking Matrices test scores in relation to height, a similar positive association is found in the random sample, but trends within social classes are more erratic. The correlation coefficients are:

Random sample ..	0·18	(P > ·01)
Classes I and II ..	−0·08	Not significant
Class III	0·14	
Classes IV and V	0·10	

Physique and Health. Patients were examined by a senior obstetrician at the time of their first antenatal clinic attendance and were graded according to general physique and health on a 5-point scale, the gradings ranging from "excellent" to "very poor". The health grading



Correlation between maternal height and test score:

·24*** ·04 ·16* ·25**

(Levels of significance: * 5 per cent; ** 1 per cent; *** 0·1 per cent)

Tall: 5 feet 4 inches and over; Medium: 5 feet 1 inch to 5 feet 3 inches; Small: under 5 feet 1 inch.

FIG. 3

Distribution of Wechsler-Bellevue intelligence test grades by Husband's Social Class and Maternal Height.

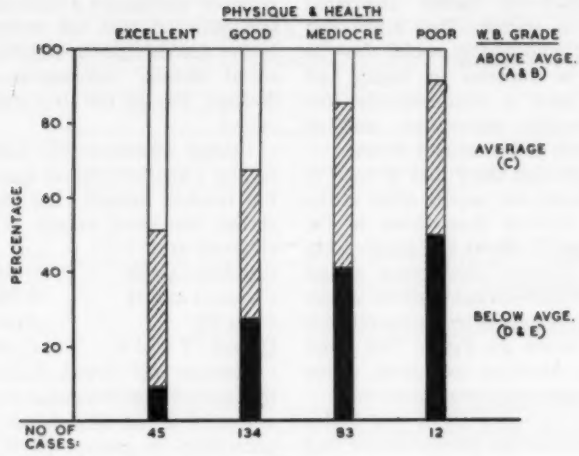


FIG. 4

Distribution of Wechsler-Bellevue intelligence test grades by Maternal Physique and Health (random sample); the physique and health of four patients was not assessed. "Poor" includes patients graded "very poor".

took place usually some weeks or months before the intelligence tests. Figure 4 shows the association in the random sample between physical health grades and Wechsler-Bellevue intelligence test grades. It is obvious that as intelligence declines the proportion of patients previously judged to have been in excellent or good health declines. Results are similar using Matrices test scores.

DISCUSSION

The fact that maternal social class, age, height and general health are fairly closely interrelated has been demonstrated by Baird (1952b). The present findings indicate that intelligence, as assessed by standard tests, forms part of the "constellation" of social and biological attributes which together are associated with reproductive efficiency. High intelligence test scores, especially with a verbal test, are more commonly obtained among older, well-grown, healthy women with a good social background and *vice versa*.

The co-existence of numerous favourable or adverse circumstances has been noted in children by the Scottish Council for Research in Education (1953): "There is at one end of the socio-economic scale, the pattern of small families, older parents, more favourable housing conditions, with children above average in intelligence and physique, and, at the other end of the scale, the large families, low housing standards, poor school attendance, and children below average in intelligence and in physical development." It is this co-existence of numerous social and biological factors which makes a social classification based on occupations such an effective tool in socio-medical research. Women who marry husbands in skilled occupations tend themselves to have been in skilled jobs and to have had a background in which skill and ability are best developed; such a background also favours good physical development and health, and hence is influential in relation to the efficiency of the physiological processes of reproduction (Illsley, 1955). But the very fact that all the various social factors which favour or militate against good health tend to be closely associated makes it very difficult to estimate the effect of each. Correlations of many kinds are easy to demonstrate, but they do not directly elucidate the problems of causation.

It seems reasonable to suppose that the possession of intellectual ability is of direct value in social adjustment and betterment;

verbal abilities especially should be valuable in understanding and responding to education in general and health education in particular. Yet it does not follow that mothers of relatively high or low intelligence will respond in essentially different ways to education; their reaction may be conditioned as much by their cultural milieu as by their individual ability. We shall discuss data in relation to this problem in the next paper of this series.

To debate the relative importance of superior social status (good environment) in producing superior physique, health and intelligence, and of superior innate quality in enabling movement up the social scale would serve no useful purpose. In human society it is practically impossible to arrange experiments in which genetically similar individuals are exposed to contrasted environments, or to demonstrate differences of genetic background by applying a similar environment to all. In practice, we must be content with the knowledge that good health is favoured by a good environment, and *vice versa*. The results of social improvements may give some clues as to the limitations imposed by genetic potential, but these limitations should not be pre-supposed.

The relationship of intelligence test scores to maternal age requires some comment. It is generally accepted that certain of the abilities measured by intelligence tests begin to decline after the age of about 25 (Wechsler, 1944); but our data show almost no correlation between age and the intelligence grades on the Progressive Matrices test; and a significantly positive correlation between age and Wechsler-Bellevue (verbal) test grades. Maternal age at the time of the birth of the first child is, of course, determined largely by social influences; the well-educated mother in the upper classes tends to marry and bear children later. The higher scores obtained among older mothers with the Wechsler-Bellevue test presumably result from social selection. This form of social selection would appear to be less influential in relation to the abilities tested by the Progressive Matrices.

Summary

It is shown that, in samples of primigravidae, higher scores obtained in two intelligence tests tended to be associated with superior social status, height and general physique and health. Higher intelligence test scores also tended to be associated with upward change of social status at marriage. The association of intelligence test scores with maternal age was equivocal; scores obtained with a verbal, but not with a non-verbal test, tended to rise as maternal age increased—an effect probably due to social selection.

The implications of these findings are discussed.

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BRENNER TUMOURS OF THE OVARY

A Report of 2 Cases Presenting Unusual Features

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THE cases here presented show pathological features sufficiently unusual to merit recording. Schiller (1934) advanced a theory regarding the pathogenesis of tumours derived from the germinal epithelium of the ovary. It is considered that the histological appearances of the first case lend considerable support to this theory.

Case 1

Mrs. L.A., para-2, aged 55 years, complained of prolapse and urgency of micturition for 1 month. For 3 weeks there had been some weakness in the right hand and shooting pains in the right arm and hand and left breast. There was no other relevant history. She had reached the menopause 10 years previously and had noticed no vaginal bleeding or discharge since that time.

On examination the patient was rather poorly nourished. There was no abnormality of the respiratory or cardiovascular systems.

Abdominal examination revealed a firm, symmetrical tumour apparently arising from the pelvis and extending to within 2 inches (5 cm.) of the xiphisternum. The patient had no idea of its existence. There was no evidence of ascites.

On vaginal examination there was a second degree prolapse and considerable vascular engorgement of the introitus and vaginal wall. The pelvis was filled by a smooth, firm mass continuous with the abdominal tumour. The uterus, which was retroverted and lying behind the tumour, appeared to be of normal size.

Laparotomy was performed 3 days later. The abdominal cavity was seen to be filled by a smooth, lobulated, pale yellow tumour which arose from the left ovary. Numerous bluish vessels were present on the surface. The right ovary appeared normal and there was no ascites.

Total hysterectomy with bilateral salpingo-oöphorectomy was performed.

From the surgical point of view convalescence was uneventful, but 2 days after operation the patient became acutely depressed and incontinent of urine. Her condition remained like this for 2 weeks. She developed a *Bacterium coli* urinary infection which responded to antibiotics; her wound healed well and there was no apparent surgical cause for this relapse.

Three weeks after operation she complained of shooting pains in the small of the back and ribs, and X-ray examination of the chest revealed multiple translucencies in the right scapula and in the ribs, some of which showed erosion. These had the appearance of metastases.

Four weeks after operation she developed faecal as well as urinary incontinence and her mental state became more confused.

As her wound had healed she was transferred to a home for incurables where she died 47 days after operation. Permission for a post-mortem examination was refused.

PATHOLOGY

The ovarian tumour, as fixed in 10 per cent formol-saline, was approximately spherical and measured 9 inches (23 cm.) in diameter and weighed 10 pounds (4·5 k.) (Fig. 1). A small part of the fimbrial end of the Fallopian tube was attached and stretched out over the surface. On external examination the tumour was

lobulated and the surface was smooth. It was pale yellow in colour.

On section the lobules, which varied in diameter from ¾ inch (2 cm.) to 4¾ inches (12 cm.) were separated by thin bands of fibrous tissue. The tumour was, for the most part, solid but there were numerous small, smooth-walled cavities which varied in size from less than 1/15 inch (1 mm.) up to ⅜ inch (1 cm.) in diameter. They appeared to be arranged chiefly at the periphery and contained a little mucinous fluid. A larger cavity, 1¾ inches (4 cm.) in diameter, was present in the middle of the tumour. Small irregular areas, white in colour, were scattered amongst the yellow tissue. The consistency of the solid part was that of hard rubber.

Microscopical sections were prepared from various parts of the tumour and were stained with haematoxylin and eosin, Van Gieson's stain, periodic acid-Schiff, and for reticulin (Fontana), fat (Scharlach R), glycogen (Best) and mucin (Southgate).

Histological Examination. Sections from different parts show that the tumour consists of nests or aggregates of epithelial-like cells separated by strands of fibromatous connective tissue. These nests of "epithelial" cells are associated with the presence of many gland spaces lined by typical columnar epithelium. Many of these glands are in active secretion. The amount of fibrous tissue is relatively small and the tumour as a whole gives the microscopical appearances of an actively functioning tissue and shows no resemblance to a fibroma, thus differing from Brenner tumours as previously described (Figs. 2 and 3).

The "epithelial" cells found in the cell-aggregates (other than the glandular epithelial cells) show considerable variation in shape and size. For the most part they are polygonal or short spindle-shaped but here and there clumps of large spheroidal cells with relatively small nuclei are present. The latter are clear cells with distended cytoplasm (Fig. 4) and in sections stained with Scharlach R are shown to contain fat. In many parts these cells are specially prominent. At the periphery of the cell nests are strands of fully-formed fibrous tissue giving the typical staining reaction of collagen. These strands give a lobulated appearance to the tumour. Sections stained for reticulin show that an extensive reticulum is present, completely surrounding the cell nests and passing between the individual cells (Fig. 5).

The glands appear to be formed by metaplasia of the cells in the cell nests. Here and there tiny clumps of cells become grouped together so as to form small rosettes. They tend to assume a more columnar shape and to develop vacuoles on the outer part of their cytoplasm. At first these cells are no larger than the other cells in the cell nests and they show a similar intensity of staining reaction. A small lumen then appears in the centre of the rosette, the columnar cells gradually become larger, stain more intensely and finally typical glands are formed. Transitional forms between these early beginnings and the mature, fully-developed glands can be easily recognized (Fig. 6). The mature glands are formed of tall columnar cells staining more intensely and standing out in marked contrast to the cells of the cell nests. They show a striking resemblance to the endometrial glands of the uterine body. In many there is well-marked vacuolation of the bases of the cells (Fig. 6) as seen in the endometrial glands in the early stages of the secretory period. In specially stained sections mucin is found only in the lumina of some of the glands and along the edge of the epithelial cells abutting on the lumen. The distribution of glycogen is patchy; it is present in all the columnar epithelial cells of some glands and is evenly distributed throughout the cytoplasm. Other glands appear to contain large amounts, particularly concentrated round the edge of the subnuclear vacuoles. It is observed occasionally in individual cells in the cell nests.

In many places large numbers of glands are present and cystic dilatations can be seen. This change is often accompanied by a disappearance of the surrounding cells and the glands are seen to be immediately surrounded by fully-formed fibrous tissue. The latter has in parts undergone a hyaline change, but deposition of calcium was not found.

The histological appearances described above are derived from the examination of some of the sections and are in keeping with those of an innocent tumour. In other sections, however,

proliferative changes of a malignant type are clearly shown. In some of these areas the glands have assumed a more complex and bizarre pattern. Many glandular invaginations are present. In places the glandular walls are formed of several layers of cells which are atypical in shape and size. The characteristic basal secretion so prevalent in the innocent areas is not found. Indeed, the appearances resemble those so frequently encountered in adeno-carcinoma of the body of the uterus (Fig. 7).

In yet other areas there is no attempt at glandular formation and the mesenchymatous tissue has undergone a change of sarcomatous type. A loose undifferentiated stroma has been formed consisting of small spheroidal or spindle-shaped cells with a number of mononucleated and multinucleated giant cells (Fig. 8).

Case 2

Mrs. E.C., para-2, aged 67 years, complained of pain in the lower abdomen for 1 year.

At the age of 49 an artificial menopause had been induced by an insertion of radium. There had been an episode of post-menopausal bleeding 10 years previously, but no tissue was obtained on curettage of the uterus.

Her present trouble had started as an occasional dragging pain in the lower abdomen made worse by effort. The pain became continuous and she noticed that her abdomen was getting large. There was a yellowish vaginal discharge.

On examination she looked fairly well for her age although she was rather obese. The blood pressure was 260 mm. of mercury systolic and 110 mm. diastolic. The heart was enlarged but there was no evidence of failure.

There was a large, cystic swelling in the lower abdomen, arising from the pelvis slightly to the right of the midline.

Pelvic examination revealed a moderate cystocele and rectocele. It was not possible to identify the uterus apart from the tumour. However, a diagnosis of an ovarian tumour was made and she was admitted to hospital.

A laparotomy was performed through a mid-line subumbilical incision. A large cystic mass was found arising from the left ovary and quite free from adhesions. The uterus and right ovary appeared normal. The cyst was tapped *in situ*, and about 3 pints (1·7 litres) of straw-coloured fluid were removed, after which the cyst was easily delivered through the incision. A bilateral oöphorectomy only was performed as her condition during the operation was giving rise to anxiety.

Her post-operative progress was uninterrupted. She has remained well since and when last seen 16 months after operation, there were no abnormal physical signs.

Pathology

After fixation in 10 per cent formol-saline, the tumour, which was approximately spherical, measured 7 inches (18 cm.) in diameter. It was a multilocular cyst, one loculus of which was much larger than the others and contained colourless watery fluid. The smaller cysts, some of which contained viscid, pale yellow fluid, were arranged round a central solid mass of white, hard tissue. The external surface of the tumour was smooth.

Sections were prepared from different portions of the tumour and stained in the same way as those from Case 1.

Histological Examination. Part of the solid portion of the tumour shows the typical appearances of a Brenner tumour of the ovary (Fig. 9). There is cyst formation in the centre of some of the epithelial clumps and the cells adjacent to this central cavity occasionally assume a more columnar appearance, but the typical epithelium of a pseudomucinous cystadenoma is not present. Special stains give reactions characteristic of a Brenner tumour. Large quantities of glycogen are demonstrated in the cells of the cell nests, but reticulin is not found between the individual cells (Fig. 10).

Sections from another part of the solid tissue show that the epithelial aggregates (cell nests) have undergone a marked change. There is considerable epithelial proliferation forming columns of cells separated by slender bundles of connective tissue. Those cells show some resemblance to squamous cells but prickle cells were not found. At the periphery of the columns the cells, which are more columnar in shape, are arranged in palisade fashion (Fig. 11). Columns of cells showing a transitional appearance between the typical Brenner "nests" and the columns above described are to be seen (Fig. 12). In other parts, however, a further change is found. The cells have become atypical and show considerable variations in shape and size. The nuclei have become hyperchromatic and giant cells of bizarre type occur. These changes indicate a possibility of malignant transformation (Fig. 13).

Comment

According to Schiller (1934) the ovarian tumours which consist of tissues never present in a normal ovary can be divided into two groups: (1) those originating from ovarian elements by wrong differentiation or abnormality in the

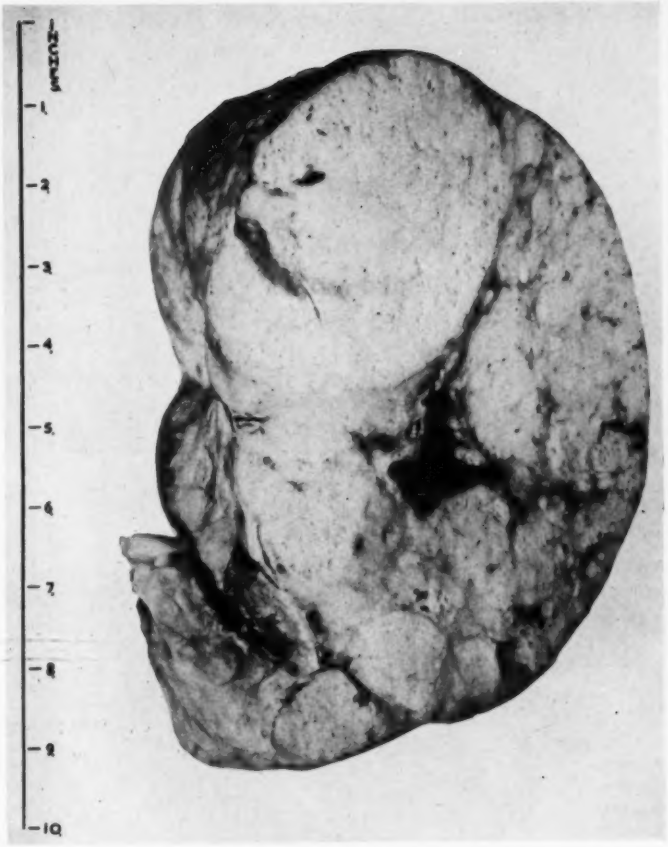

FIG. 1
Case 1. Bisected tumour. $\times \frac{1}{3}$.

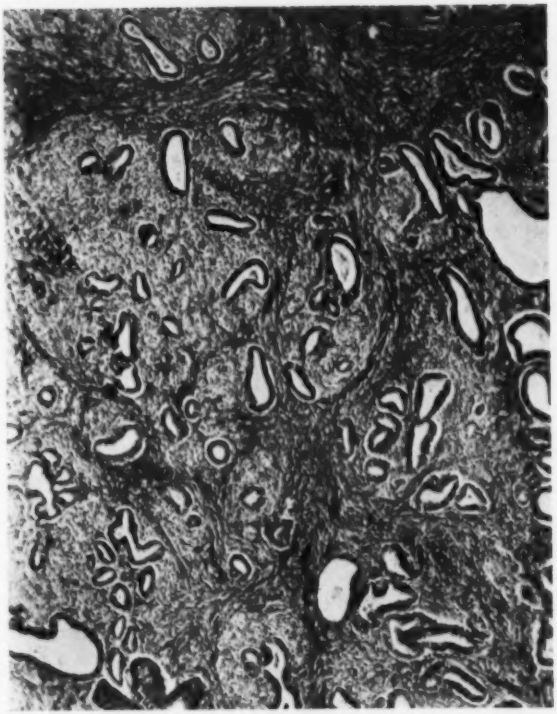

FIG. 2

Case 1. Benign portion of tumour showing glands surrounded by aggregates of cells. H. & E. ×42.

FIG. 3

Case 1. Higher magnification of gland and surrounding cells. H. & E. ×240.

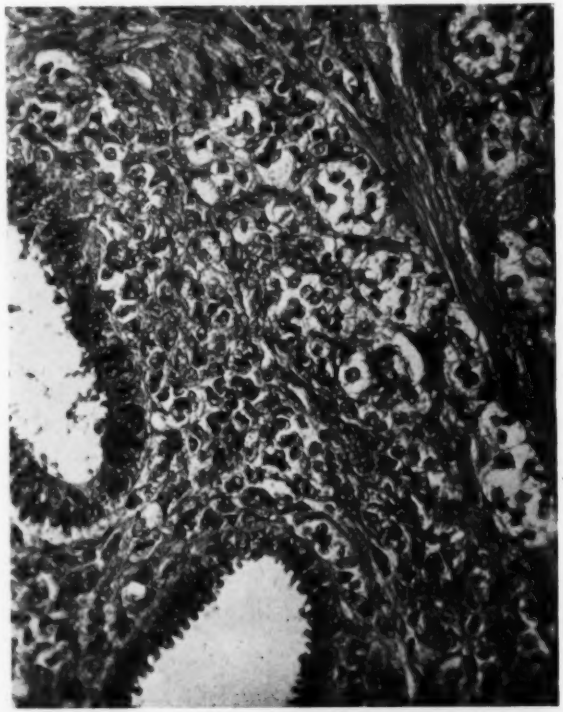

FIG. 4

Case 1. Large cells with clear cytoplasm at periphery of cell "nests", shown to contain anisotropic fat. H. & E. ×240.

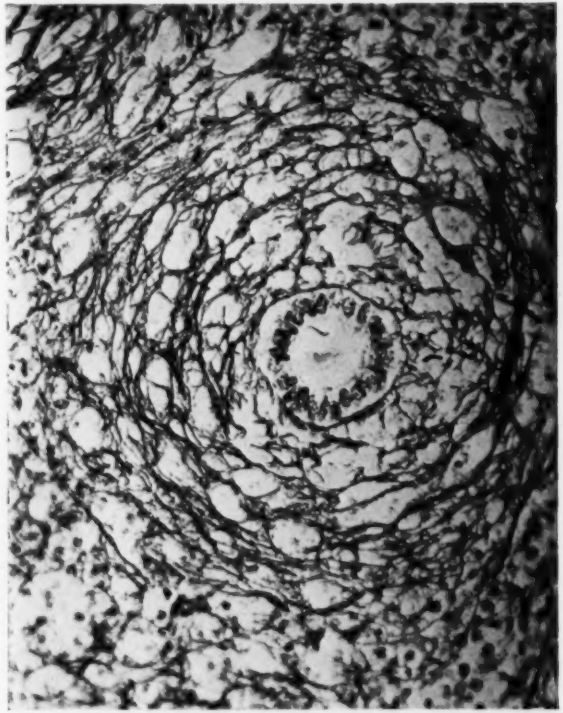

FIG. 5

Case 1. Section stained to show reticulin particularly between the individual cells of the cell "nests". Reticulin. ×240.

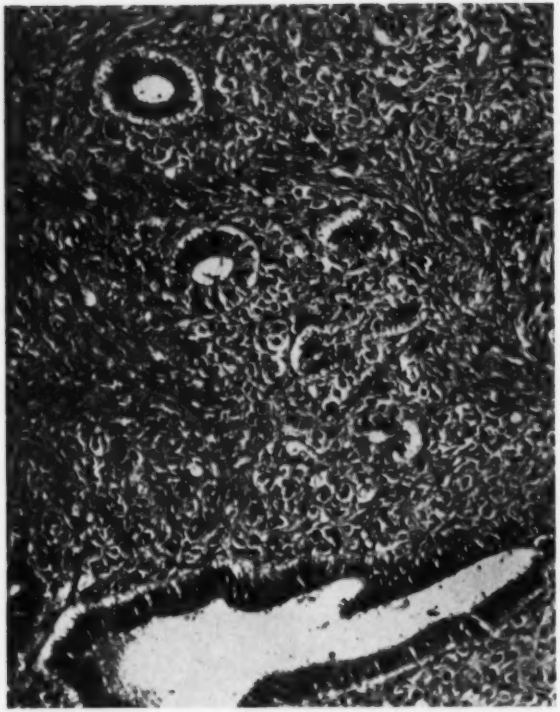

FIG. 6

Case 1. Apparent differentiation of "stromal cells" into glands. Vacuolation in the mature glands is easily seen. H. & E. ×140.

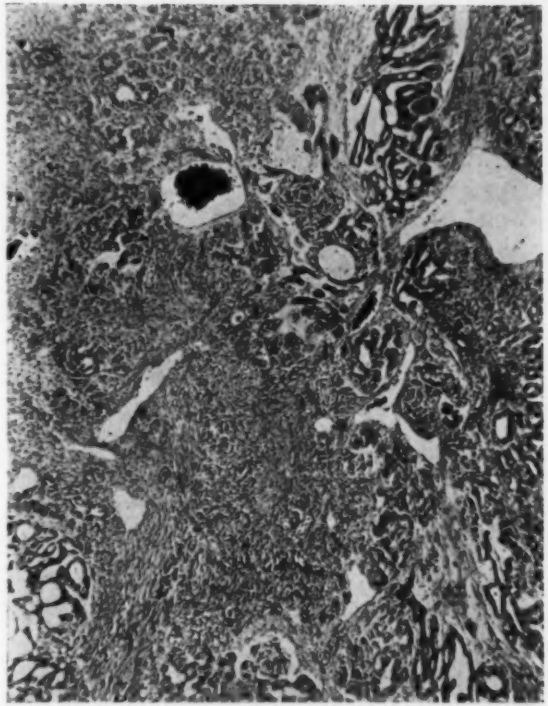

FIG. 7

Case 1. Carcinomatous part of tumour which shows great similarity to adenocarcinoma of the endometrium. H. & E. ×90.

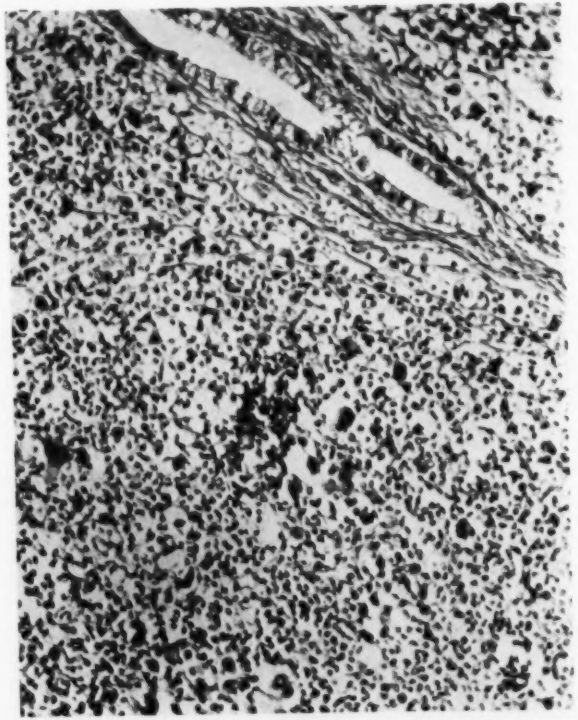

FIG. 8

Case 1. Sarcomatous part of tumour containing many large, bizarre giant cells. H. & E. ×140.

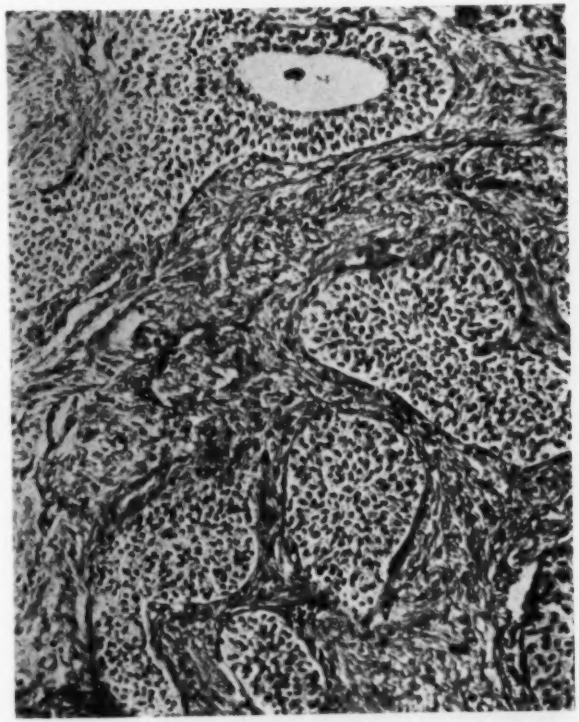

FIG. 9

Case 2. Typical appearances of a Brenner tumour seen in some areas. H. & E. ×140.

J.B., K.R.D., G.W.G.

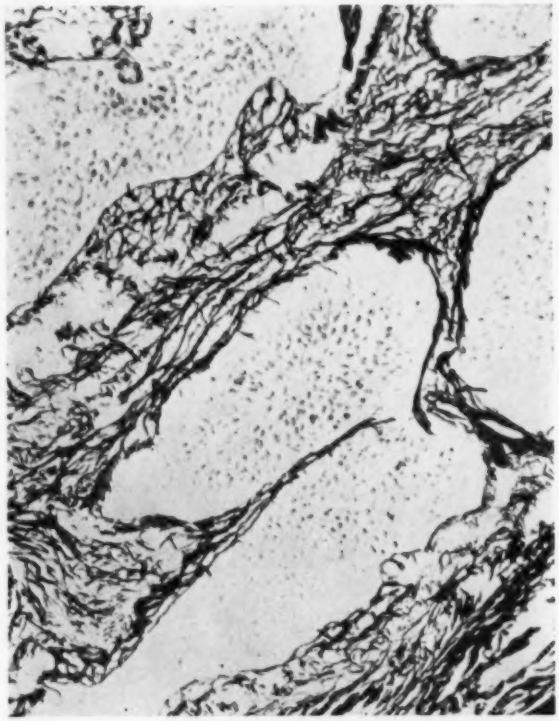

FIG. 10

Case 2. A similar area stained to show reticulin. Reticulin. ×140.

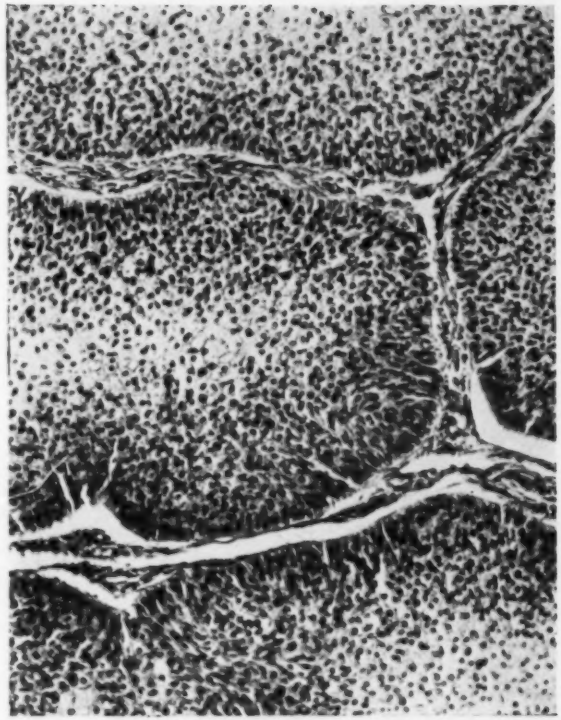

FIG. 11

Case 2. Hyperplastic epithelium resembling squamous epithelium. H. & E. ×140.

FIG. 12

Case 2. Part of the tumour showing transition from the appearances of Fig. 9 to Fig. 11. H. & E. ×40.

FIG. 13

Case 2. Atypical epithelial proliferation with giant cells suggesting carcinomatous change. H. & E. ×140.

chromosomes, and (2) those developed from cells which are dislocated into the ovarian parenchyma.

On this basis the Brenner tumour is usually classified in the second group. He states that the Brenner tumour "consists of islands of transitional epithelium surrounded by non-specific fibrous tissue. The islands may enclose glands or little cysts lined with high columnar epithelium. Even if either the first or the third component is missing, the tumour is classified as a Brenner tumour." Novak and Jones (1939) consider there are two essential constituents in a Brenner tumour, viz., "the characteristic nests of epithelial cells" and "the fibromatous connective tissue groundwork surrounding the epithelial islands". On these counts, therefore, the tumour in Case 1 should be regarded as a Brenner tumour. In most tumours, but not in all, there is a tendency to central cystic degeneration of the epithelial nests. In some cases there results a small central cavity containing a rounded mass of degenerated protoplasm resembling an ovum. In others the small central cavities may be lined by a tall columnar mucoid type of epithelium like that of the pseudomucinous cystadenoma and it is considered that large cystadenomata may arise in this way.

Greene (1952) considers that there are 4 possible modes of origin:

(*a*) From Walthard's rests, which are inclusions of epithelial cells probably derived from the surface epithelium of the ovary.

(*b*) From the epithelium of the rete ovarii. Schiller (1934) demonstrated a continuity between the epithelium of a Brenner tumour and that of the rete ovarii. He considers that the rete in this case is abnormal because there is continuity between it and the Wolffian tubules. Such continuity, however, has been found by Greene in 11 out of 13 serially sectioned broad ligament specimens.

(*c*) From the stroma of the ovary by a process of metaplasia. Greene describes 8 tumours of this type. All are grossly of the solid fibroma-like variety and the formation of cystic spaces is not a marked feature. He notes apparent transitions between the stromal cells and the epithelial cells of the cell nests.

(*d*) Directly from the germinal epithelium of the ovary.

The ovarian tumour presented here (Case 1) appears to show unusual and peculiar features as compared with the great majority, if not all, of the Brenner tumours hitherto described. Some Brenner tumours are very small, even of microscopical size, whilst others may be extremely large. The largest solid Brenner tumour appears to be that of Neiman (1936) which weighed 15 pounds (6·8 kg.). In this case the tumour weighed 10 pounds (4·5 kg.). The amount of fully-formed fibrous tissue constituting the framework of the tumour is relatively very small compared with that of the epithelial islands. From the histological point of view it shows no resemblance to a fibroma of the ovary, a resemblance found to a marked degree in many tumours previously described. In many cases of Brenner tumours there is a tendency to cyst formation in many of the epithelial islands. The cysts may be lined by irregular cells in the process of degeneration or, as in some tumours, by a layer of cubical or columnar cells. In this case, however, there is an extensive formation of functionally active glands, the epithelium of which, in those fully developed, stands out in bold contrast to the cells of the epithelial islands. The glands do not resemble those of a pseudomucinous cystadenoma but show a remarkable resemblance to endometrial glands. Many show vacuolation of the bases of the epithelial cells like the endometrial glands in the early stage of the secretory period. Stained for mucus and for glycogen the glandular epithelial cells show similar reactions to those of the endometrium.

It might be asked whether this is a case of ovarian endometrioma. If so, it would be most unusual. Most ovarian endometriomata of moderate size form chocolate cysts which in this case do not exist, and moreover there is no other evidence of haemorrhage. The epithelial islands in this tumour show little resemblance to the stroma cells of the endometrium, in which the large clear cells containing fatty material are rarely seen. These cells containing anisotropic lipoid have been observed in the epithelial nests in other Brenner tumours. In a case studied some years ago the presence of many

solid epithelial nests composed entirely of clear cells constituted a definite feature in the histological picture. We have been unable to find any transition between the fibromatous connective tissue and the epithelial cells of the cell nests as observed by Greene. In this case also there was penetration of reticulum into the epithelial masses, a condition found by Greene only in those Brenner tumours which he considers to be of stromal origin. We would prefer to regard the epithelial cell nests as derived from stroma cells, and consider that the glands are formed by metaplasia from them as shown in Fig. 6. An analogy can be drawn between this process and the formation of tubules from the stroma in Wilm's tumour of the kidney as suggested by Cappell (1951). The analogy with this developmental tumour of the kidney is increased by the sarcomatous changes described above.

A survey of the literature has revealed only occasional cases of malignant Brenner tumour. Dubrauszky and von Massenbach (1947) and Dubrauszky (1949) have recently described 2 such neoplasms. The histological findings in this tumour show that malignant transformation has taken place, and this is supported by clinical observations and X-ray examination. It is to be regretted that permission for autopsy, which might have afforded additional evidence, was refused.

It is, of course, impossible in a tumour of this size to find an origin from Walthard's rests or from the rete ovarii. We would prefer to believe that this tumour belongs to Schiller's first group, i.e., originating from ovarian elements by wrong differentiation or abnormality in the chromosomes. The potentialities of the coelomic cells are widespread. Thus Schiller states "cells from the surface epithelium of the ovary with erroneously preserved Müllerian potencies if shifted by folds to the depths of the albuginea may differentiate to a type of epithelium normally found in the products of the Müllerian duct. Tubal differentiation leads to serous cystomas with linings of serous and ciliated columnar epithelium: uterine differentiation to endometriomas: cervical differentiation to pseudomucinous cystomas."

In Case 2 the changes occurring in the cell nests have taken place in a different direction suggesting an early carcinomatous change without any tendency to glandular formation. A number of tumours of this type have been described and illustrated recently by Teoh (1953).

Summary

Two ovarian tumours considered to belong to the category of Brenner tumours are described. The first presents features of a very unusual type and it is thought to represent a rare form of differentiation of the ovarian stroma cell in the direction of endometrium. The second tumour, which has been described chiefly for purposes of comparison, is more traditional in type.

We are indebted to Mr. A. J. Wrigley for permission to publish Case 1, and Mr. N. A. Richards who provided the case history. Our thanks are also due to Mr. A. E. Clark for the photomicrographs, and Mr. A. L. Wooding for Figure 1.

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TWO CASES OF INTRAPERITONEAL HAEMORRHAGE FOLLOWING NORMAL DELIVERY

BY

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INTRAPERITONEAL haemorrhage following normal delivery is an unusual complication and in view of this and the unusual cause of the bleeding we are reporting these two cases. In both instances a haematoma formed in the posterior vaginal fornix and ruptured through the peritoneum into the pouch of Douglas. These patients were delivered within a month of each other in the Royal Maternity Hospital, Belfast.

The first patient, seen by one of us (R.A.E.M.), was a third para whose first pregnancy terminated in a normal delivery. The second pregnancy was complicated by a Type III placenta praevia and a classical Caesarean section was performed at 38 weeks.

At the third pregnancy the antenatal period was uneventful and she came into labour spontaneously at the 38th week. She was allowed to proceed in labour and after an initial period of indefinite pains began to have very strong contractions which dilated the cervix up from 5/– dilatation to full dilatation in half an hour. One of us (R.A.E.M.) was with her at this time and observed a normal delivery, conducted by a pupil midwife, of a baby weighing 5 pounds 11 ounces. The perineum was intact and the third stage completed without event in 15 minutes. There was no post-partum haemorrhage. The pulse rate following delivery was 88 and the blood pressure 140/80.

Delivery occurred at 11 p.m. and the following morning at 4 a.m. a moderate loss occurred for which ergometrine was given.

Later in the morning she developed severe abdominal pain and marked shoulder tip pain. There was extreme tenderness all over the abdomen most marked low in the iliac fossae. The uterus was tender but well contracted and not larger than normal for this stage. There was pain on deep breathing. Vaginal bleeding had now returned to normal. The pulse rate was 94 and rose gradually to 120. The blood pressure remained at 140/84. The temperature was 100·4° F.

It was apparent that there had been intraperitoneal haemorrhage, and this diagnosis was made. In view of the previous classical section the possibility of a ruptured uterine scar was considered although we were not satisfied from the clinical picture that this was the cause.

Laparotomy was performed and free blood with clot was found in the peritoneal cavity. The old uterine scar was intact and the seat of the bleeding was found to be a haematoma on the posterior vaginal wall. The bleeding appeared to have ceased and suturing was not carried out. The abdomen was closed after clots had been removed. The patient was placed in the lithotomy position while still under the anaesthetic and the cervix found to be quite intact. A 1½ inch linear tear was found in the posterior fornix and deep to this was a haematoma. As there was no bleeding sutures were not inserted.

The patient made a good recovery.

The second case was a patient aged 33 years. At her first confinement in 1952 she developed pre-eclamptic toxaemia for which a surgical induction of labour had to be carried out at 38 weeks. The placenta and membranes appeared to be complete but 9 weeks later she had a secondary post-partum haemorrhage and a portion of placenta was found to have been retained.

Her second pregnancy was uneventful during the antenatal period and she came into labour on the 9th April, 1955 delivering herself spontaneously as an occipito-posterior of a baby weighing 9 pounds 13 ounces. The placenta and membranes were delivered spontaneously but it was thought that one cotyledon was deficient and, in view of the previous experience mentioned above, the uterine cavity was explored manually to make sure that no portion of the placenta was retained. The

delivery occurred at 10.20 p.m. on the 9th April. At 5 a.m. on the 10th April, having slept comfortably following delivery, the patient woke up with severe pain in both shoulders. Her blood pressure was 120 and she was not complaining of any abdominal pain. On being propped up the pain disappeared from the shoulders but was now localized in the lower abdomen. The patient at this stage was seen by a colleague and it was thought that she had had some intraperitoneal bleeding, but on account of the level of her blood pressure the abdomen was not explored and it was felt that the intra-peritoneal bleeding had ceased.

On the 11th April, i.e., 36 hours after delivery, the patient was still very uncomfortable with some abdominal distension, but there was no fall in blood pressure and the pulse was 90. The abdomen was therefore explored and found to contain approximately 1½ pints of blood which was mainly in the upper part of the abdomen. At first no sign of a bleeding point could be demonstrated, but later an area in the posterior vaginal fornix showed evidence of a haematoma which had evidently ruptured 5–6 hours after delivery.

As no further bleeding was occurring from this area sutures were not inserted. There was no evidence of any laceration in the vaginal fornix itself. Following this the patient had some degree of ileus but after 48 hours made an uninterrupted recovery.

Discussion

These two cases presented some difficulty in differential diagnosis. In the first case a previous Caesarean section had been performed and the possibility of a ruptured uterine scar had to be considered. The clinical appearance of the patient and her general condition were rather against this diagnosis.

In the second case a ruptured uterus could be eliminated because the uterine cavity had been explored immediately after delivery of the placenta.

In both cases the general condition, pulse rate and blood pressure ruled out the possibility of a ruptured splenic vessel, but both cases are similar in that they had to be explored without a definite diagnosis having been made.

In the first case the rapidity of the second stage of labour may have resulted in the vaginal laceration and the formation of the haematoma, but it is difficult to explain why the bleeding occurred intraperitoneally rather than *per vaginam*.

In the second case it is difficult to explain why the patient should develop a haematoma in the posterior fornix apart from the size of the baby and the presentation. This combination may have caused over-distension and subcutaneous laceration of the vaginal fornix. Against this theory is the fact that in the first case where a similar complication occurred the baby weighed only 5 pounds 11 ounces.

LOCALIZED CONGENITAL DEFECTS OF THE SCALP

BY

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LOCALIZED congenital defects involving the whole thickness of the hairy scalp are of comparatively rare occurrence and their aetiology is obscure. Terruhn (1930) reviewed 76 cases and by 1953 there were 150 cases in the literature.

Localized scalp defects are usually located over the vertex but they may be on the occiput or behind the ear. More than half the defects are in the mid-line and over 80 per cent are near or in this position. In 70 per cent of the cases the defect is single; in 20 per cent double and in 8 per cent triple. Females are in the preponderance and in a little over half of the cases the affected child is the first-born (Ingalls, 1933). As a rule the lesions are small and are one to two cm. in diameter, but they may be as large as nine cm. in diameter (Heidler, 1924). Skin defects are commoner on the scalp than elsewhere on the body. Whilst collecting 76 cases of scalp defects, Terruhn (1930) found only 26 cases of skin defects elsewhere in the body. In common with other congenital defects, a foetal cutaneous deficiency is often only one of several co-existent anomalies. Among the deformities associated with scalp defects are hydrocephalus, microphthalmus, meningocele, hare lip and cleft palate, and coloboma, and in the limbs a variety of conditions (Heidler, 1924).

CLINICAL TYPES

Localized congenital scalp defects are of two main types and these are exemplified by the following cases.

(1) *The Circular Type*

Case 1.—Mrs. F.E., aged 28 years, expected her first baby on 23rd May, 1954. Labour commenced spontaneously on the 24th May, and, following an uneventful labour, a male infant weighing 6 pounds 11 ounces was born with white asphyxia. The infant responded rapidly to resuscitation and it was noticed to have a scalp lesion.

A circular deficiency was present in the scalp 1¼ inches in diameter a little to the right of the mid-line over the posterior fontanelle (Fig. 1). The whole thickness of the scalp was replaced by a thin transparent membrane having the appearance of amnion. Beneath this thin membrane, the dura mater could be seen clearly with the superior longitudinal sinus in the mid-line. The vault of the skull was absent in this region and for ¼ inch around the circular defect, i.e., the underlying posterior fontanelle was enlarged and was 1¾ inches in diameter. The membrane could be moved quite freely upon the underlying dura mater and a small vein passed from the edge of the defect immediately beneath the membrane and entered the superior longitudinal sinus. The edge of the defect was clearly defined, slightly raised, devoid of hair and was white in colour with small haemorrhagic areas.

A second small scalp deficiency, 3 mm. in diameter was present in the mid-line, 2½ cm. behind the larger opening.

No other congenital abnormalities were present.

The mother of this infant, Mrs. F.E., had an indurated area of scar tissue on her scalp, 1 inch in diameter, devoid of hair and sweat glands and overlying the lambda (Fig. 2). She gave a history of having a scalp deficiency at birth which had healed spontaneously 3 weeks later. On clinical examination no underlying bony defect was felt and an intact skull vault was confirmed by X-ray. No other cases of scalp deficiency had occurred in the family.

Treatment

The surrounding scalp was shaved and the defect covered with a tulle gras dressing. The lesion, which bulged considerably when the child cried, was protected by a padded watch spring pessary. Four days later the opening was ¾ inch in diameter and healing rapidly. The scalp was completely healed a month after birth.

In this circular type of defect, the lesion is usually confined to the skin (Abt, 1917; Anderson and Novy, 1942; Calloway *et al.*, 1946) but occasionally it may include bone (as in this case) and may penetrate to the dura mater (Kehrer, 1910; Calloway *et al.*, 1946; Terruhn,

1930). In a case described by Terruhn, the defect was symmetrical and extended through the skin, periosteum and bone to the cerebral membranes and allowed the convolutions of the brain to be clearly seen. Greig (1931) considered that such an extensive affection was so unusual that it was possibly of a totally different aetiology.

(2) *The Linear Type*

Defects of this type are elongated or stellate rather than circular and often overlie one of the suture lines of the skull. The sagittal suture together with the anterior and/or posterior fontanelles appear to be the areas usually involved (Pincherle, 1938). In this type the suture lines are widened, and, when fontanelles are involved, these too are enlarged.

Case 2.—Mrs. M.S., aged 38 years, expected her third baby during January, 1955. Labour commenced spontaneously on 9th March and an uneventful delivery of a male infant weighing 7 pounds 7 ounces occurred 3 hours later.

A linear deficiency of the scalp was present extending backwards for 3 inches in the mid-line from the anterior fontanelle. The posterior end of the defect extended laterally over the right parietal bone for ¾ inch (Fig. 3). The anterior 1½ inches of the lesion was covered by thin wrinkled skin as if healing had recently taken place and the surrounding skin was reddened. The posterior half of the lesion was covered by a thin crinkled, glistening membrane, black in colour due to diffusion of blood on its deep aspect.

X-ray examination of the skull revealed widening of all the suture lines and fontanelles, but no defect of the right parietal bone was present beneath the posterolateral extension of the scalp defect. The head circumference of this infant was 13¾ inches. Apart from a left sided hydrocele no other congenital defects were present.

Treatment

Tulle gras dressings were applied for 5 days after which a dry adherent scab formed over the posterior part of the lesion and this was exposed to the air. The hard crust remained attached for 6 weeks when spontaneous separation took place, to reveal the wound smaller but still unhealed. A second crust formed and the condition remained unchanged until the baby was 4 months old. A small amount of bright red bleeding then occurred and the infant was re-admitted to hospital where saline dressings resulted in separation of this second scab without further haemorrhage. Wound healing slowly took place until a further small secondary haemorrhage occurred in the 27th August, 1955, the infant being now nearly 6 months old. After this the lesion healed without further incident.

Histology

In neither of the 2 cases described was excision of the lesion undertaken and there was no opportunity to observe the microscopic anatomy of the lesions. Bonnaire and Durante (1913) described the membrane as being made up of flat, very thin, nucleated cells, regularly set out in one layer, appearing as a rudimentary epithelial covering. Neumann's (1924) cases are particularly instructive because excision of the affected areas permitted histological examination. The rim around the raw surface was composed of many layers of epithelium, deep to which the subcutaneous connective tissue was normal with sebaceous glands and hair follicles. The defect itself was covered by a membrane composed of a single layer of squamous or cubical cells, deep to which the tissue was necrotic in places with red blood corpuscles, leucocytes and fibroblasts in its structure.

Aetiology

The earlier theories favoured amniotic adhesions as a cause (Kehrer, 1910). In discussing intra-uterine amputations in general, Streeter (1930) concluded that amniotic bands do exist and are sometimes associated with malformations, but, where this has occurred, the two had participated in the same disturbance and the latter were not mechanically produced by the former. Greig (1931) concluded that localized scalp defects were due to arrest of development because:

(1) It is difficult to see why amniotic bands should have any symmetrical attachments or should have a predilection for the scalp.

(2) The bulla or ulcer is frequently mid-line.

(3) In most cases no band or remnant of a band is found on inspecting the placenta and membranes at birth.

(4) The same defect has occurred in the same position in two successive children in the same family (Campbell, 1826).

Mechanical injury has been suggested as a cause of these defects, e.g., by the use of instruments to rupture the membrane. This is clearly not so, for in most cases no instrumentation had been performed and in one of

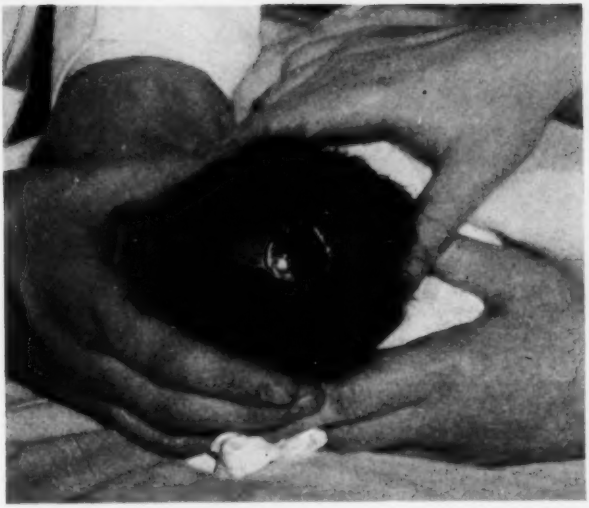

FIG. 1
Case 1. Infant with circular scalp defect one day old.

FIG. 2
Scalp of Mrs. F. E., aged 28 years, mother of the infant shown in Fig. 1.

FIG. 3
Case 2. Infant with linear scalp defect one day old.

D.S.

Neumann's cases (1924) the child was delivered by hysterotomy.

Babies with congenital scalp deficiencies are particularly susceptible to cerebral trauma caused by vaginal instrumentation performed during labour. Figure 1 shows how easily perforation of the brain might have taken place had induction of labour by a Drew-Smythe catheter been performed.

I have seen a number of infants born with small punched out ulcers of the scalp. These are about ½ cm. in diameter and their floor is covered with a red glistening membrane. They heal within the first 4 days of life. In all these cases the foetal membranes have ruptured spontaneously, and instrumentation cannot be incriminated as the cause of the scalp lesion. These are undoubtedly congenital scalp deficiences of a minor degree.

Diagnosis

Kahn and Olmedo (1950) describe how Dr. Russell Atchison was called to a delivery in Northville, Michigan. He had been told by the attending nurse that the membranes had ruptured. It was a vertex presentation and on inspection of the vulva he naturally took the presenting shining scalp defect for unruptured membranes. He reached for a haemostat and was about to open them when fortunately the patient had a severe labour pain and with further bulging he suddenly realized that this was the infant's head presenting.

Heredity

Campbell (1826) observed that the condition occasionally occurred in more than one member of the family. He described a congenital scalp defect as follows:

"In the space intermediate to the posterior angle of the bregma and the occipital extremity of the sagittal suture, a point of the integument, the size of a crown piece, presented the appearance of having been the seat of an ulcer."

On the eighth day after delivery this child died from bleeding from the superior sagittal sinus underlying the ulcer. To the same parents 3 years later a male child was born in whom an ulcer of the scalp was present 20 mm. posterior to the vertex in the sagittal plane. At eight months of age, this child died from "hydrocephalus of a chronic variety".

Kahn and Olmedo (1950) describe a large congenital scalp defect occurring in a fourth sibling. The first 2 children had been normal but the third and fourth had entirely similar scalp defects. There were no known instances of similar anomalies in this family and the parents were not related. Kahn and Olmedo were of the opinion that the occurrence of 2 children with so similar and well-defined a defect from one marriage in a large family group, strongly suggested that the condition was due to a recessive gene; in which case the chances would be one in four that any subsequent child would be likewise affected.

Tisserand-Perrier (1953) has described scalp defects occurring in three generations of one family.

In Case 1 described here, the mother and baby had scalp lesions in identical situations, i.e., over the posterior fontanelles (Fig. 1 and Fig. 2). From the size of the mother's scar, it is estimated that both scalp defects were about the same size at birth.

Treatment

Congenital scalp defects which are small will cicatrize in a short time, thus providing adequate cover (Terruhn, 1930). The scar may be excised later for cosmetic reasons. This is seldom necessary and in Case 1 the scar was completely hidden by hair. Van Eycken (1952) described a healed defect in a two and a half year old boy, excised because of an embarrassing absence of hair.

In Pincherle's case (1938) the lesion which was the size of a copper "centave" was replaced in 10 months by an exostosis.

In larger defects, however, particularly if they lie over the superior sagittal sinus, there is danger of necrosis followed by haemorrhage with meningitis and subsequent death in either event. Peer and Van Duyn (1948) describe a scalp defect overlying the sagittal sinus, in which death due to haemorrhage occurred 8 weeks after birth. Death from haemorrhage has taken place in 4 other cases and in all the cases the lesion was of the linear form, relatively large and lay over the superior sagittal sinus. The sequence of events was as follows: first, a dry gangrene of the membrane characterized by blackening and

mummification; then, detachment at the edge followed by bleeding and death. Usually, but not always, there were several preliminary haemorrhages before the final one. The two secondary haemorrhages, which occurred at the 4th and 6th months in Case 2 described here, were unusually late in their occurrence. Peer and Van Duyn (1948) conclude that if the lesion is larger than 1–2 cm. at birth, and lies over a widened suture, it may become necrotic. If the superior sagittal sinus is exposed by detachment of the crust, a fatal haemorrhage is likely to follow. In such cases surgical closure of the defect is advisable.

Kahn and Olmedo (1950) described a scalp defect 5×7 cm., rhomboidal in shape, extending from the anterior to the posterior fontanelle. They closed the defect with rotation flaps, the scalp being undermined as far as possible in all directions. The operation was performed under local anaesthesia and large venous sinusoids were controlled by electro-coagulation. (A striking feature on histological examination of this specimen was the occurrence of calcification of the hair follicles in the atrophic portion of the scalp, sebaceous and sweat glands being absent.)

In the untreated case, where a large crust of necrotic material is already present, and one haemorrhage has already occurred, Peer and Van Duyn (1948) suggest that ligation of the superior sagittal sinus on both sides of the lesion might be considered as a preliminary step to excision of gangrenous areas and plastic reconstruction. In the second case described here, the lesion was relatively small when secondary haemorrhage occurred at the fourth month. The bleeding was small in amount and because of this a more conservative line of treatment was undertaken.

Of Ingalls' (1933) 60 cases, collected from the literature of all types of scalp defect, the mortality, including stillbirths, was 20 per cent, most of the deaths being more or less directly referable to the scalp lesion.

Summary

Localized congenital skin defects of the scalp are rare, and when present commonly occur over the vertex. Two main forms are recognized —the circular and the linear—and an example of each type is described. Minor degrees of this condition take the form of small punched out ulcers.

The condition is occasionally familial and a case is described in which a mother and her infant had similar lesions at birth. The cause of these defects is unknown but it is thought to be due to a recessive gene rather than amniotic adhesions and bands. Instrumentation plays no part in the aetiology of this condition, but the lesion exposes the underlying brain to damage, e.g., by the passage of a Drew-Smythe catheter.

In the absence of infection, healing takes place rapidly and the aim of treatment is the avoidance of the twin dangers of meningitis and haemorrhage. If the defect is large and involves the sagittal suture, secondary haemorrhage is likely, and in such cases early surgical closure is advisable.

I wish to thank Dr. C. T. Potter, Consulting Paediatrician at Kingsbury Maternity Hospital, for permission to publish these cases, and I am indebted to Mr. Muir, of the Mount Vernon Hospital Plastic Surgery Unit, for his helpful advice regarding the treatment of these two infants.

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AMENORRHOEA: AN ANALYSIS OF CASES SEEN AT A GYNAECOLOGICAL ENDOCRINE CLINIC*

BY

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AND

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THE cases of amenorrhoea that are presented and analyzed are those that have been seen over the past six years at the Endocrine Clinic of a large and purely gynaecological hospital. Most of the patients attending the clinic were referred by other members of the staff, all of whom are gynaecologists. Thus the emphasis is on the gynaecological side, and the patients in the series to be described were referred primarily because of the amenorrhoea. As a result, the cases naturally tend to be selective, and it can be understood why certain types are so poorly represented. Thus few cases would be expected of amenorrhoea secondary to general systemic disease, such cases being sent to a general hospital; similarly, those cases associated with some gross endocrine disorder, such as Cushing's syndrome, diabetes and thyrotoxicosis, are also more usually sent to a general hospital, whether it be to an endocrine clinic or to the general medical out-patient clinic.

In the course of analyzing our cases of amenorrhoea the need for a comprehensive classification of this disorder soon became apparent. Although many papers have been written over the past twenty years on the subject of amenorrhoea, most of these deal each with a single aspect and make no attempt to present any classification. Classifications of amenorrhoea are infrequent, not only in papers on the subject but also in textbooks and monographs, both of gynaecology and of endocrinology. Those examples that we have been able to find proved inadequate for our purpose, as so many of our cases were difficult to classify under existing headings. Further, there is considerable discrepancy and disagreement between various classifications, due largely to the differing particular interests of the workers concerned. It was thus necessary to devise a broad and general classification that would also include all the conditions encountered in our series and yet not be too detailed.

In planning the classification the usual broad separation into primary and secondary amenorrhoea was employed. The term primary amenorrhoea was applied to women of 18 years of age or over who had never menstruated. Secondary amenorrhoea was applied to women under the age of 40 who complained of amenorrhoea of at least 3-months duration, whether they had previously menstruated normally for some years or had only bled scantily and on a few occasions in their lives.

We suggest the following classification:

PRIMARY AMENORRHOEA

A. SEXUAL INFANTILISM

No sexual development and no secondary sex characteristics—by the age of 18 years.

(1) *Primary Pituitary*

Including: chromophobe adenoma, craniopharyngioma and asexual ateleiotic dwarfism; selective FSH deficiency; Fröhlich's syndrome (a hypothalamic lesion although it may be associated with a pituitary tumour).

(2) *Primary Ovarian*

Including ovarian agenesis and Turner's syndrome; disease of ovaries, such as tuberculosis and sepsis.

* Based on a paper given to the Endocrine Club, Glasgow, on 10th December, 1954.

(3) *Other Endocrine Disorders*
Such as cretinism and juvenile myxoedema.

B. Sexual Hypoplasia (Hypogonadism)
With poor sexual development and slight secondary sex characteristics only—by the age of 18 years. (Often with short stature, and probably representing a degree of hypopituitarism; sometimes representing merely a delay in development.)

C. Absence of Menarche
With sexual development and secondary sex characteristics. ("Physiological" up to the age of 18 years.)

(1) *No Endometrial Development*
(*a*) With normal sized uterus which will respond to oestrogen.
(*b*) With hypoplastic uterus; but with little or no hypoplasia elsewhere.
(*c*) Disease of uterus but with normal uterine development; such as endometrial tuberculosis.
(*d*) With normal uterine development and no evidence of disease of uterus, but with no response to oestrogen: uterine insensitivity.

(2) *With Proliferative Endometrium*
Delay in onset of ovulation.

(3) *Psychogenic*
Fear, environmental change, etc. (probably acting through the hypothalamus and usually associated with anovulation).

(4) *Obesity* (*simple*)
May be associated with anovulation or with no endometrial development.

(5) *Cryptomenorrhoea*
Associated with a vaginal septum.

D. With Abnormal Sexual Development
Hermaphroditism; pseudohermaphroditism (adrenogenital syndrome), and Cushing's syndrome.

Secondary Amenorrhoea

In a woman, under 40, who comes complaining of amenorrhoea and who has had it for three months or more.

A. General or Systemic
(1) Nutritional: starvation and anorexia nervosa. (The effect of these may be generalized or the action more specific through the pituitary with gonadotrophin deficiency.)
(2) Chronic infections, etc., such as tuberculosis, generalized or pulmonary; chronic nephritis, and malignancy.
(3) Intoxications, such as lead, alcohol and drugs.
(4) Anaemia and other blood diseases.
(5) Other endocrine disorders: thyroid disorders (usually hyperthyroidism); diabetes; Addison's disease; adrenogenital syndrome; Cushing's syndrome.

B. Psychogenic
Fear, worry, sudden fright, etc. Change of climate or of environment. (Probably all anovulatory and acting through the hypothalamus.)

C. Obesity
Usually associated with anovulation and a proliferative endometrium but may be associated with an inactive atrophic endometrium.

D. Pituitary
Simmonds's disease, as in post-partum necrosis; tumour: including chromophobe and chromophil adenomata.
Persistent lactation:
(*a*) Chiari Frommel syndrome (always post-partum and associated with hyperinvolution of uterus).
(*b*) "Spontaneous" (may or may not be associated with a preceding pregnancy).

E. Pituitary-ovarian
(1) Primary hypofunction—with poor sexual development in general (bleeding probably having occurred only scantily and on a few occasions).
(2) Secondary hypofunction ("ovarian failure")—with previous normal menstrual history.
(3) Anovulation (with a proliferative endometrium).

F. Ovarian
Disease (destructive):
(*a*) Infection, such as tuberculosis and sepsis.
(*b*) Tumour, such as Krukenberg's tumour.
Stein-Leventhal syndrome with bilateral cystic ovaries.
Arrhenoblastoma.
Removal by surgery; destruction by irradiation.

G. Uterine
Disease: endometrial tuberculosis; puerperal sepsis. Destruction as a result of a previous curettage. Insensitivity. Cryptomenorrhoea (due to cervical stenosis). (Hysterectomy.)

H. Pregnancy and Physiological Lactation

I. Premature Menopause
Distinguishable from secondary hypofunction (ovarian failure) by the presence of menopausal symptoms.

Primary Amenorrhoea

Some comments are desirable with regard to certain points in the classification. The age of 18 was chosen as the earliest for accepting the definition of primary amenorrhoea, in order to

eliminate as far as possible cases merely of slight delay in development. This applies particularly to those cases showing the less severe defects, such as would be included under the category of sexual hypoplasia or of absence of menarche. There is also the difficulty before a certain age of classifying a case as one of sexual infantilism, since it may later fall into the less severe category of sexual hypoplasia; but by the age of 18 this is much less likely to occur.

The term asexual ateleiotic dwarfism is applied to the so-called pituitary dwarf, a diminutive person with normal proportions, with no secondary sexual development and with low urinary FSH excretion. The aetiology of this condition is usually difficult to determine; some cases are associated with nutritional defect, such as coeliac disease, and others appear to be congenital and probably due to some primary pituitary defect. Selective FSH deficiency represents sexual infantilism without dwarfism; the cases are usually rather tall with typical eunuchoid proportions and are differentiated from the similar picture of eunuchoidism due to primary ovarian defect by low urinary FSH excretion. The patients with sexual infantilism due to primary ovarian causes may either be short or tall in stature, the latter with typical eunuchoid proportions. The former are examples of ovarian agenesis, the stunting of growth being genetic, and in both examples the urinary FSH excretion is raised.

With regard to the second group, that of "Sexual Hypoplasia", it was obvious as soon as we came to analyze our own series that there was a considerable number of patients who were certainly not cases of sexual infantilism and yet were more than cases merely showing a hypoplastic uterus. They appear to lie between these two groups, indicating varying degrees of hypogonadism. All our cases were rather short in stature, with normal proportions; and in all the cases where urinary FSH was estimated this was found to be low. These facts suggested a degree of hypopituitarism and we looked upon this group as probably representing delayed development due to hypopituitarism, some of whom would probably develop all right, as in fact did occur in some of the cases in our series, while others might remain deficient all their lives.

The cases classified under the heading "Absence of Menarche" represent the best developed of the first three groups, all patients having normal or nearly normal female figures. Those with a proliferative endometrium are the nearest to normal, representing anovulation and probably merely a delay in the onset of ovulation. Those showing no endometrial development are stages in hypoplasia, probably representing an inequality in response; thus some girls start to menstruate very early while their breasts are still small and undeveloped, whereas others may have extremely well-developed breasts but have a hypoplastic uterus and menstruation may not start for a few years.

Investigation of patients with primary amenorrhoea always included a thorough medical examination for evidence of general systemic disease as well as for evidence of other endocrine disorders. Careful measurements were taken to determine body proportions. X-rays of skull and of long bones for epiphyseal development were done routinely. An examination under anaesthesia was usually advised—except in certain cases of group C (absence of menarche) —where there was reason to expect merely a delay in or absence of ovulation. In those cases chorionic gonadotrophin was given, 1,500 International Units by injection daily for 5 consecutive days. If there was no bleeding after these injections or where curettage was carried out and no endometrium was obtained, an "artificial period" was usually given, the details being as follows: on the 1st, 3rd, 5th, 8th, 10th, 12th, 15th, 17th and 19th days Oestradiol Benzoate, 50,000 International Units was given by injection. With the 8th injection, 10 mg. progesterone was given. With the 9th injection, and on the five consecutive days following the 9th injection, 15 mg. progesterone was given.

Out of a total of 176 cases of amenorrhoea there were 30 patients with primary amenorrhoea. The cases were made up as follows:

Sexual Infantilism: 6 cases

Primary Pituitary: 4 cases: Chromophobe adenoma (1); Ateleiotic or pituitary dwarf (1); Selective FSH deficiency (2).

Primary Ovarian: 2 cases: "Idiopathic" (? ovarian agenesis) (1); Tuberculous salpingo-oöphoritis (1).

Sexual Hypoplasia (hypogonadism): 11 cases

Absence of Menarche: 12 cases

With no endometrial development: 9 cases: With normal sized uterus (1); With hypoplastic uterus (5); With normal sized but insensitive uterus (3).

With proliferative endometrium: 2 cases.

Obesity (simple): 1 case.

Abnormal Sexual Development: 1 case.

Virilism (adrenogenital syndrome).

The patient with the chromophobe adenoma was a girl of 19, slightly undersized and with no secondary sexual development. She has developed well with replacement therapy which has included oestrogen implants. Surgery is now being considered because of commencing visual field defect. The case of ateleiotic or pituitary dwarfism was a small, elf-like child of 21 years of age who is still being treated with small doses of thyroid only, in the hope that further growth will occur. The exact aetiology of her condition has not been established. The 2 cases of selective FSH deficiency were tall, thin girls of 26 and 29 years of age respectively, with typical eunuchoid figures and no secondary sexual development. In both cases the FSH excretion was less than 20 mouse units/diem. These 2 patients have received replacement therapy with oestrogen implants and now show good secondary sexual development. One of the two cases of sexual infantilism due to primary ovarian causes had genital tuberculosis. She had a typical eunuchoid figure but her FSH excretion was low, less than 20 mouse units/diem, which might be explained by her tuberculous infection. The other case was a girl of 19 years of age with normal stature and proportions, but with no secondary sexual development. She had had hot flushes for 3 years and her urinary FSH excretion was 60 mouse units/diem. It was considered that she probably had an unexplained developmental defect of the ovaries.

The 11 cases of sexual hypoplasia (hypogonadism) ranged in ages from 18 to 22 years. They were all short statured, 5 being under 4 feet 10 inches in height, but all 11 had normal proportions. In all the cases where FSH was estimated (5 patients), it was found to be low, less than 20 mouse units/diem. There were 5 cases exceeding 5 feet in height and in all of these treatment was directed to their genital development only. Three of these cases were found to be sensitive to oestrogen, one of whom started to bleed cyclically on her own after responding to an "artificial period". Two of the cases were found to be insensitive to oestrogen. Of the 6 cases under 5 feet, one was given oestrogen implants on two occasions and within 2 years was bleeding cyclically on her own. One was given thyroid in small dosage and one implant of oestrogen. There was good effect both of growth and of sexual development, but no bleeding has yet occurred. Four cases were given thyroid only since it was considered that growth in stature was the more important factor. In 2 cases there was very considerable improvement both in growth and development but no bleeding has yet occurred in either. One case is too recent yet to assess, the other has shown little or no improvement.

Among the 12 cases with absence of menarche the one patient with no endometrial development, but with a normal-sized uterus, bled satisfactorily after an "artificial period": she was later found to have a dysgerminoma. Of the 5 patients with hypoplastic uteri, 2 had "artificial periods" and not only bled satisfactorily after these but continued to bleed cyclically on their own thereafter; 2 others also received "artificial periods", one of whom bled satisfactorily after each of three, but did not bleed on her own. The other did not bleed even after three courses of injections. The fifth patient was given an implant of oestrogen but it is too early to assess the effect of this. Of the 3 patients with normal-sized but insensitive uteri, none bled after three or more "artificial periods" and endometrial biopsies repeated after the courses of injections still showed no endometrial response.

Both the cases with a proliferative endometrium bled after injections of chorionic gonadotrophin, one continuing to do so

cyclically on her own thereafter. The case of obesity did not have an endometrial biopsy performed, but she bled satisfactorily after an "artificial period". Weight reduction was also advised but she subsequently defaulted. The case of virilism was a girl of 20 years of age of very small stature and with no secondary sex development and gross facial and body hirsutism. She had had gross clitoral enlargement, but this organ had been amputated before she was seen at the clinic. 17-ketosteroid excretion was very high, and bilateral adrenal hyperplasia had previously been confirmed at laparotomy. This patient has shown considerable breast development and has bled vaginally, continuing to do so fairly regularly since commencement of cortisone therapy.

Secondary Amenorrhoea

Out of the total of 176 cases of amenorrhoea in the present series, 146 were of secondary type. The cases in this group were made up as follows:

Pituitary-ovarian hypofunction ..	87 cases
Obesity	29 cases
Anovulation	8 cases
Galactorrhoea	5 cases
Endometrial tuberculosis	4 cases
Psychogenic causes	4 cases
Pituitary necrosis	2 cases
General or systemic conditions ..	2 cases
Destruction of ovarian function ..	2 cases
Insensitive uterus	1 case
Disease of uterus	1 case
Premature menopause	1 case

The initial investigation of these cases of secondary amenorrhoea consisted of a thorough general examination, particular attention being paid to the exclusion of endocrine conditions. Where feasible, pelvic examination and endometrial biopsy were also carried out at the Endocrine Clinic, but in quite a number of cases this was not possible, as many of the patients were young, unmarried girls. In such cases, where endometrial biopsy was later judged necessary, admission to hospital was arranged and the procedure was carried out under general anaesthesia. The subsequent management varied with the condition present, and reference will now be made to each of these categories in turn.

(1) *Pituitary-ovarian Hypofunction*

In analyzing the cases of secondary amenorrhoea, it was seen that by far the largest number seemed to be examples of varying degrees of sexual hypofunction. But it was difficult to determine whether the primary defect was in the pituitary or the ovary. For this reason the term "Pituitary-ovarian Hypofunction" was used to describe this group. The 87 cases can conveniently be divided into primary and secondary types.

(a) *Primary hypofunction:* 34 cases. The patients in this group had never had a normal menstrual cycle. Menstruation was at best scanty and infrequent, and, in some of the more marked cases, only a few periods had occurred over a number of years. On pelvic examination, the uterus was invariably found to be small, and general sexual development was usually poor. Endometrial biopsy was carried out in 21 of these patients, with the following results:

No tissue obtained	12 cases
Inactive proliferative endometrium	4 cases
Atrophic endometrium ..	2 cases
Cystic glandular hyperplasia	1 case
Irregular ripening of endometrium	1 case
Secretory phase of cycle ..	1 case

The initial treatment consisted of either an "artificial period" or of chorionic gonadotrophin, depending on the circumstances of the individual case. Subsequent management depended on the initial response to these measures. The results can be grouped as follows:

Bled after some form of artificial period	11 cases
Bled after chorionic gonadotrophin	3 cases
Failed to bleed after chorionic gonadotrophin, bled after artificial period	5 cases
Failed to bleed after chorionic gonadotrophin, bled after endometrial biopsy ..	1 case
Bled after endometrial biopsy only	1 case

Failed to bleed after chorionic gonadotrophin, then defaulted	3 cases
No result. Defaulted or too early in follow-up	10 cases

It will be seen that at least one menstrual period occurred in all patients who continued to attend for any length of time. Although the number of defaulters was large, 3 of the relatively small number who attended regularly continued to menstruate without further treatment.

(b) *Secondary hypofunction:* 53 cases. All the patients in this category had had normal menstrual periods for at least a few consecutive months, and in many cases for a number of years. In every instance the uterus was found to be small, and general sexual development was frequently though not invariably poor. Endometrial biopsy was carried out in 38 of these patients, with the following findings:

No tissue obtained	21 cases
Atrophic endometrium ..	8 cases
Inactive proliferative endometrium	6 cases
Secretory endometrium ..	2 cases
Cystic glandular hyperplasia	1 case

The initial treatment was on similar lines to the primary hypofunction group, an "artificial period" or chorionic gonadotrophin being given according to the circumstances of the individual case. Subsequent management depended on various factors, including the response to the initial measures. The results can be grouped as follows:

Bled after some form of artificial period	19 cases
Bled after chorionic gonadotrophin	1 case
Failed to bleed after chorionic gonadotrophin, bled after artificial period	6 cases
Bled after endometrial biopsy only	4 cases
Bled spontaneously without treatment	3 cases
Failed to bleed after chorionic gonadotrophin, then defaulted	4 cases
No result. Defaulted or too early in follow-up	16 cases

It will thus be seen that every patient in this group who attended for any length of time bled at least once. Again the number of defaulters was large, but, of the relatively small group who continued to attend for a reasonable length of time, 4 continued to bleed regularly, and one later became pregnant. The patients who reported return of normal menstruation before treatment was started are excluded from this group.

(2) *Obesity*

There were 29 cases of obesity associated with amenorrhoea. In some of these the obesity was only of short duration, but frequently it had been present for some years. The increase in weight sometimes came on after pregnancy. In other cases there was no apparent reason, and several patients said that it followed marriage. The duration of the amenorrhoea varied from 3 months to 4 years. Endometrial biopsy was carried out in 12 cases in this group, 7 showing an atrophic endometrium and 5 an inactive proliferative endometrium of anovulatory type. Weight reduction was advised in all cases, the patient usually being put on an 800 calory diet, frequently with Dexedrine in addition. In a few instances, use was also made of chorionic gonadotrophin or of "artificial periods". The results in the obesity group can be divided into 4 categories:

(*a*) Very successful. 12 cases. Following weight reduction, the menstrual periods returned and the patients subsequently had what appeared to be normal regular cycles. Three of these patients later became pregnant, 2 after more than 6-months amenorrhoea. Eight of these patients had dieting only, 2 had diet and chorionic gonadotrophin, and 2 had diet and "artificial periods".

(*b*) Temporary success. 3 cases. Bleeding did occur after weight reduction, but a normal cycle was not restored.

(*c*) Unsuccessful. 2 cases. Weight reduction was satisfactory, but bleeding did not return.

(*d*) No result. 12 cases. Most of these patients defaulted, but in a few it is as yet too early to assess the result.

It will be seen from these figures that the type of secondary amenorrhoea associated with abnormal gain in weight offers a much better prospect of cure than the type associated with genital hypofunction.

(3) *Anovulation*

Eight cases. The patients in this group had ceased to ovulate, but could usually be stimulated by chorionic gonadotrophin to bleed. Five of the 8 patients had an endometrial biopsy, all showing an inactive proliferative endometrium. All 5 were given chorionic gonadotrophin, 4 bleeding thereafter; the fifth patient showed a well-developed proliferative endometrium before chorionic gonadotrophin but did not bleed. Three of these 5 patients continued to bleed cyclically on their own and one defaulted. The other 3 did not have an endometrial biopsy, but all bled after chorionic gonadotrophin, 2 continuing to do so and one defaulting.

(4) *Galactorrhoea*

Five cases. All the patients in this group were married, parous women, and all 5 showed some degree of obesity and gave a history of gain in weight. In 3 of these the amenorrhoea persisted after the birth of a child. In each instance the uterus was small for a parous woman, the length of the cavity being 2½ inches, but it is doubtful if they are true examples of the Chiari-Frommel syndrome. In one further case the uterus was of normal size and the fifth patient was found to have a chromophobe adenoma of the pituitary. In all 5 cases an "artificial period" was given and bleeding followed. The chromophobe adenoma was removed successfully, but in this, as in the other 4 cases, the galactorrhoea persisted in spite of various forms of treatment. These results are in keeping with the present view that there is no curative treatment for this interesting condition.

(5) *Tuberculosis of the Endometrium*

There were 4 patients with endometrial tuberculosis, 2 being unmarried. There was no history of previous pregnancy in any case. Although we do not, as a routine measure, carry out endometrial biopsy in every unmarried girl with amenorrhoea, we feel that it is necessary to do so where chorionic gonadotrophin has produced no bleeding, particularly where the secondary sex characters are well developed and there is nothing to suggest hypofunction. Failure to carry out this procedure in such cases will involve the risk of missing occasional examples of endometrial tuberculosis. All 4 patients have since been included in a large scale investigation into various aspects of genital tuberculosis in women. Each has received a course of streptomycin and PAS and subsequent endometrial biopsies have shown that the tuberculous infection has not recurred. An interesting feature of this group is that normal menstruation was restored in all 4 patients following treatment of the tuberculous condition.

(6) *Psychogenic Causes*

There were 4 patients in this group, aged from 18 to 26 years. In one case the amenorrhoea dated from a fall, in 2 others from a fall from a bicycle, and in the fourth case from seeing a sister fall from a bicycle. This association with bicycles is interesting, but the number of cases is too small to enable us to draw any conclusions. Two of these patients showed proliferative endometrium on biopsy; both bled after an "artificial period", and both later developed cystic glandular hyperplasia. The other 2 had atrophic endometrium on biopsy; one bled after an "artificial period" and continued to bleed normally without further treatment, the other bled only after an "artificial period".

(7) *Pituitary Necrosis*

There were 2 patients in this group, one with typical Simmonds's disease who had had amenorrhoea for 4 years, the other with Simmonds's disease and diabetes insipidus.

(8) *General or Systemic Conditions*

In this group there was one case of Felty's syndrome, a form of rheumatoid arthritis, and one case of hyperthyroidism. Both patients were referred to a general hospital for medical treatment.

(9) *Destruction of Ovarian Function*

Two cases. One patient had amenorrhoea following previous removal of both tubes and

ovaries for pelvic tuberculosis. The other had amenorrhoea following deep X-ray therapy for Hodgkin's disease. Both patients complained of hot flushes.

(10) *Insensitive Uterus*

There was only one example of insensitive uterus in the whole series. This patient was aged 23 years and complained of amenorrhoea of 18-months duration. No tissue was obtained on endometrial biopsy. Three "artificial periods" were given without result and a second endometrial biopsy also failed to produce any tissue. This patient was not obese.

(11) *Disease of Uterus*

The one patient in this category complained of amenorrhoea of 17-months duration, following a septic abortion. No tissue was obtained on endometrial biopsy and there was no bleeding after an "artificial period". It seems probable that the amenorrhoea in this case is permanent.

(12) *Premature Menopause*

The only patient in this category had amenorrhoea with well-marked menopausal symptoms. Bleeding occurred following both chorionic gonadotrophin and "artificial periods", but the menopausal symptoms persisted and the periods did not recur. She was aged 35 years and had had amenorrhoea for 10 months.

Conclusions

Some writers have questioned the advisability of treating patients with amenorrhoea. It is considered, however, that the results obtained in the present series amply justify the measures employed. In spite of the fact that a large number of patients defaulted in the early stages, bleeding was induced by one or other form of treatment in most cases, and menstruation was re-established on an apparently normal basis in a substantial number. The psychological effect of restoration of bleeding, even temporarily, has been most beneficial and, in a few cases, the subsequent occurrence of pregnancy is proof of restoration of normal function. In addition, this investigation has brought to light a number of conditions requiring general medical or surgical treatment, such as endometrial tuberculosis.

THE SPERM ANTI-AGGLUTINIC FACTOR IN WOMEN

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SPERM anti-agglutinic factors were discovered in sperm plasm, and in secretion from the tubes in cattle by Lindahl and Kihlström in 1952. The male factor, later found in man, horse, swine and rabbit, was isolated and further studied (Lindahl and Kihlström, 1954a and b; Kihlström, 1954; Lindahl and Edlund, 1955). The female factor, which up to now has been less studied, was found in growing follicles of cattle, swine and rabbits. In rabbits it is produced in the tubes during oestrus or following gonadotrophic stimulation of the ovaries by hormone injections or mating (Lindahl and Nilsson, 1954). Both factors are non-species-specific in their biological action. They are inactivated when oxidized, but regain their biological activity at reduction.

This investigation has been carried out in order to give a guiding review concerning the physiological occurrence of the sperm anti-agglutinic factor (A.A.F.) in women and its significance for clinical work in obstetrics and gynaecology.

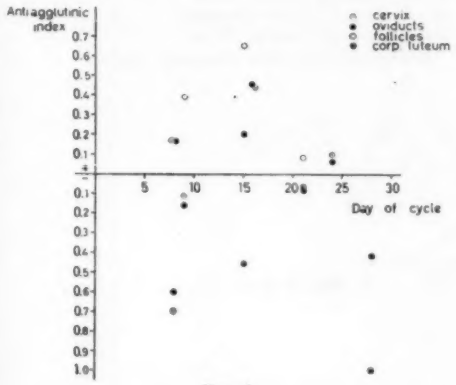

FIG. 1

Anti-agglutinic indices of different secretions from eight normally menstruating women.

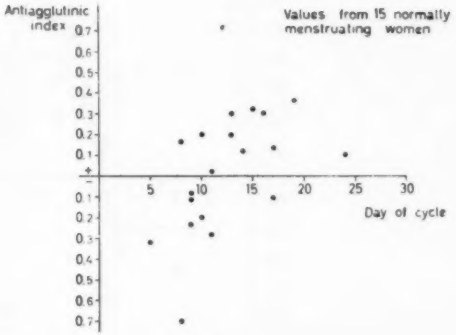

FIG. 2

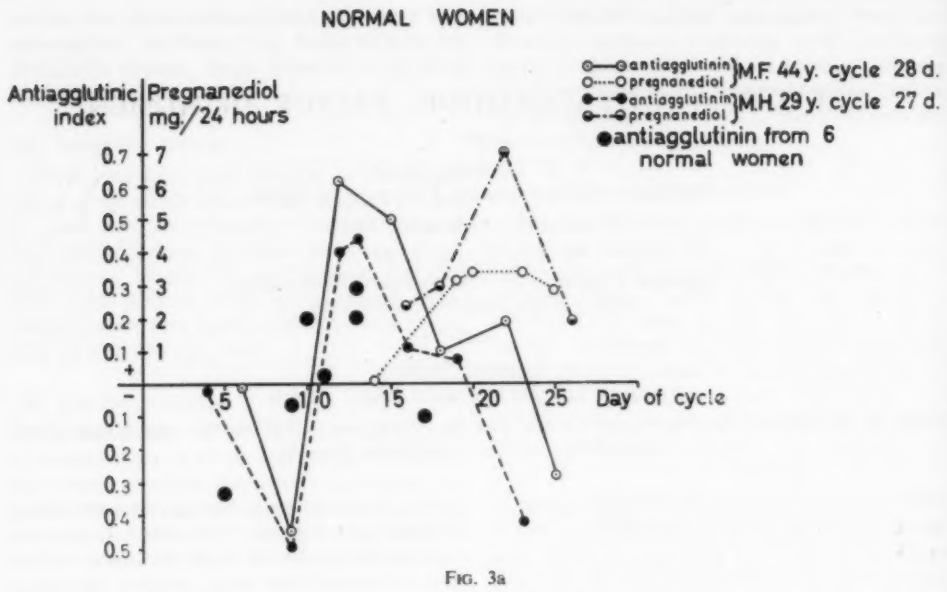
NORMAL WOMEN
antiagglutinin } M.F. 44 y. cycle 28 d.
pregnanediol }
antiagglutinin } M.H. 29 y. cycle 27 d.
pregnanediol }
antiagglutinin from 6 normal women
Antiagglutinic index
Pregnanediol mg./24 hours
0.7 7
0.6 6
0.5 5
0.4 4
0.3 3
0.2 2
0.1 1
+
5 10 15 20 25 Day of cycle
0.1
0.2
0.3
0.4
0.5

FIG. 3a

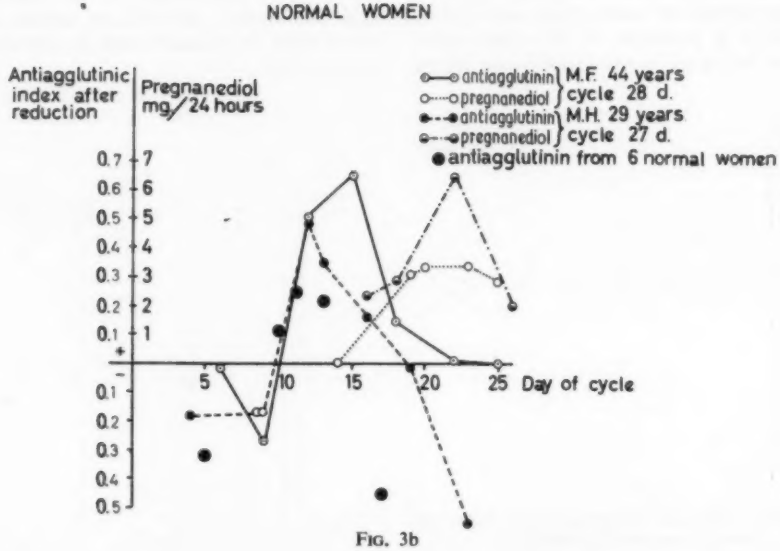
NORMAL WOMEN
Antiagglutinic index after reduction
Pregnanediol mg./24 hours
antiagglutinin } M.F. 44 years
pregnanediol } cycle 28 d.
antiagglutinin } M.H. 29 years
pregnanediol } cycle 27 d.
antiagglutinin from 6 normal women
0.7 7
0.6 6
0.5 5
0.4 4
0.3 3
0.2 2
0.1 1
+
5 10 15 20 25 Day of cycle
0.1
0.2
0.3
0.4
0.5

FIG. 3b

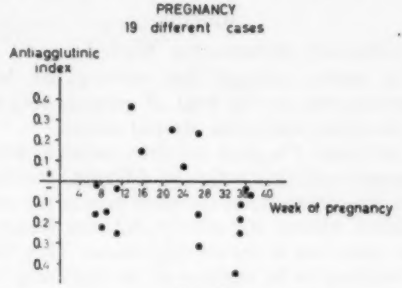

FIG. 4

MATERIAL AND METHODS

The cervical mucus has been aspirated as completely as possible in different phases of the menstrual cycle of normal women, in normal pregnant women, in normal post-menopausal women, after salpingectomy, after salpingo-oöphorectomy, after treatment with hormones, and in cases of sterility. In suitable cases of laparotomy cervical mucus and follicular fluid have been aspirated. As the oviducts do not contain free fluid enough for aspiration 0·5 ml. of physiological saline has been injected into the abdominal os of the tube and aspirated again after one minute. This fluid was examined for anti-agglutinic activity in the same way as the other secretions.

The biological technique for the determination of the A.A.F. has been described previously (Lindahl and Kihlström, 1954a). An anti-agglutinic index (A.A.I.) has been calculated according to the following formula

$$1 - \frac{\text{per cent sperm heads agglutinated after addition of the sample}}{\text{per cent sperm heads agglutinated before addition of the sample}}$$

This index has been calculated as it is easy to use in clinical work. The standard error of the method *per se* is about ± 10 per cent. The varying amounts of dry substance in the secretions have not been considered, and sometimes, especially when the secretions are very mucous, the determination may be difficult. It is therefore impossible to give an exact value of the combined sources of error in a given case. Thus the numerical values of the A.A.I. must not be exaggerated.

Determinations of the urinary excretion of oestrogens and of pregnanediol have been made according to methods published by Furuhjelm in 1940 and 1953 respectively.

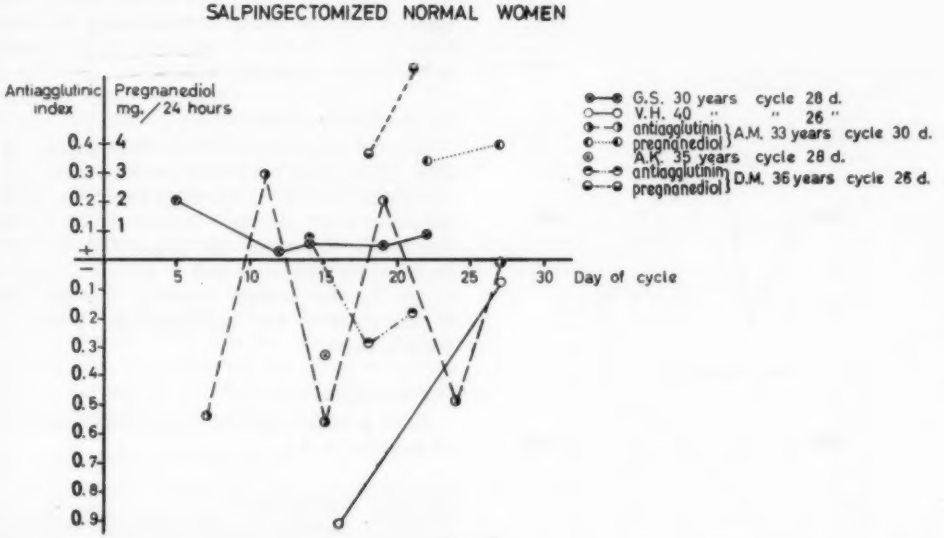

FIG. 5

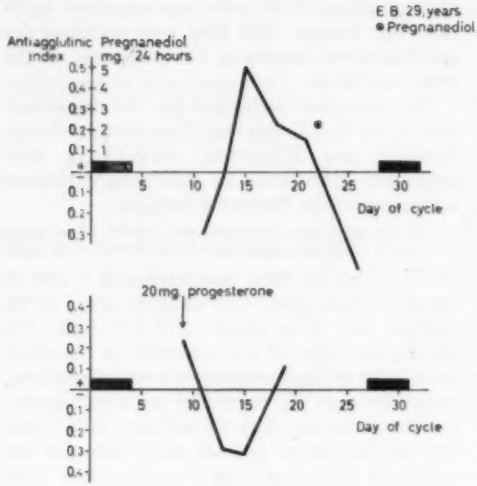

FIG. 6

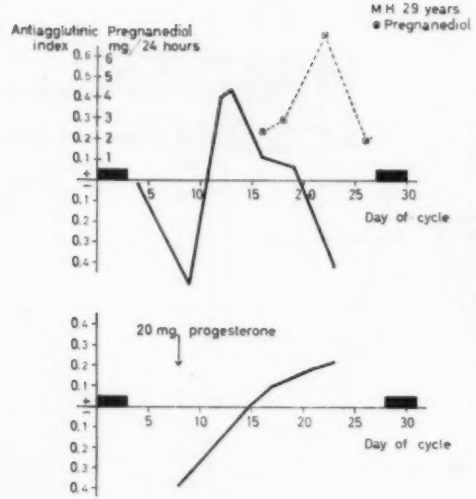

FIG. 7

RESULTS

(1) *Normally Menstruating Women*

A sperm anti-agglutinic activity has been demonstrated in the fluid of growing follicles, in the tubes, and in the cervical mucus.

In Figure 1 8 cases are demonstrated, where the anti-agglutinic action of different secretions has been examined at the same time in the same patient. Almost the same A.A.I. are found in the tubes and in the cervical mucus. They have a tendency to be negative at the beginning and at the end of the menstrual cycle, but are positive in the middle. The fluid of growing follicles has a positive index. However, as soon as corpus luteum formation takes place the index becomes negative. Positive values are also found in Figure 2, collected from the cervical mucus of 15 normally menstruating women, and in Figure 3a, where 2 normal women have been followed through a complete menstrual cycle and 6 different women have been examined one or two times during the same cycle. In the introduction it was mentioned that the A.A.F. is inactivated when oxidized. Figure 3b demonstrates the values of the women of Figure 3a after the cervical mucus has been reduced by treatment with sodium thioglycollate 1:10,000. Almost the same A.A.I. are found demonstrating that the bulk of the A.A.F. is present in the active reduced form in normal women.

(2) *Normal Pregnancy*

Cervical mucus from 19 normal women in different phases of pregnancy has been examined. The same A.A.I. is found without or after reduction with sodium thioglycollate. From Figure 4 it is evident that negative A.A.I. are found at the beginning and at the end of pregnancy. In the middle, however, the cervical mucus inhibits the agglutination, giving a positive index.

(3) *Menopause*

The 8 post-menopausal women examined had all negative A.A.I.

(4) *After Salpingectomy*

Only 4 salpingectomized normally menstruating women have been examined as it was not

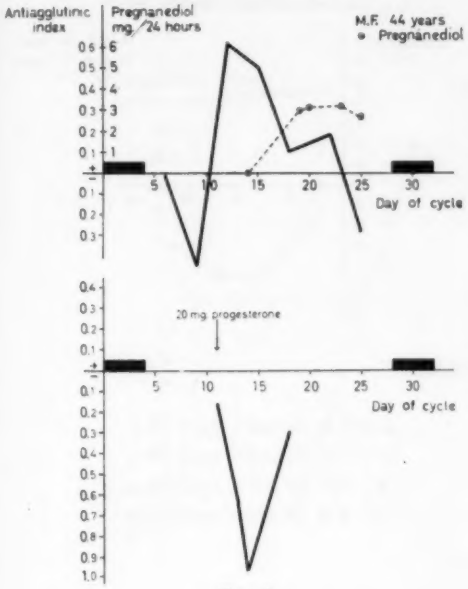

FIG. 8

possible to get more suitable cases. They had been sterilized due to various social or psychical conditions. In one case fertility had later been wanted. One ovary was then removed, and the other one was implanted in the fundus uteri. Their A.A.I. are seen in Figure 5. After reduction of the cervical mucus the same values were found. They are negative or only slightly positive, and do not show the cyclic changes of the normal women. Case G.S. has a positive value on the 5th day of the cycle probably due to contamination with sperm plasm following co-habitation the night before. The two positive values of case A.M. may be caused by follicle ruptures as the surface of her ovary was lying free in the uterus. She had significant excretion of pregnanediol a few days later.

(5) *After Hormone Treatment*

In 3 normal women the A.A.I. of the cervical mucus was determined on several occasions during a menstrual cycle, and the urine was examined for pregnanediol (Figs. 6, 7, 8). They had all their highest A.A.I. at the time of ovulation, and their lower or negative indices in the first part of the cycle and during the secretory phase. The following cycle they were given an injection of 20 mg. of progesterone a few days before the time of ovulation. The A.A.I. then became strongly negative instead of positive.

Figure 9 demonstrates the values from 3 post-menopausal women. Following an injection of 10 mg. of oestradioldiproprionate the A.A.I. of the cervical mucus is increasing.

Five normal post-menopausal women were given 20 mg. of progesterone (Fig. 10). At the time of injection the A.A.I. was negative. In 2 cases determinations were made after 2 and 3 days. At that time the A.A.I. had decreased

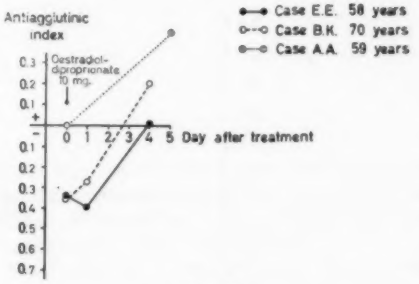

FIG. 9

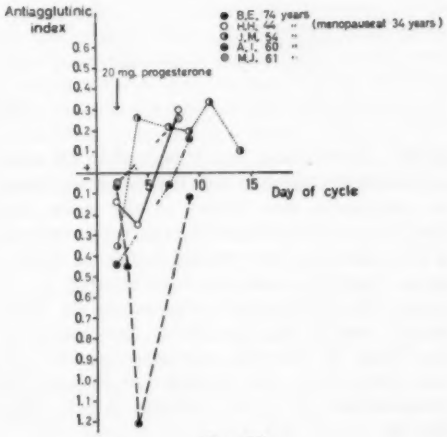

FIG. 10

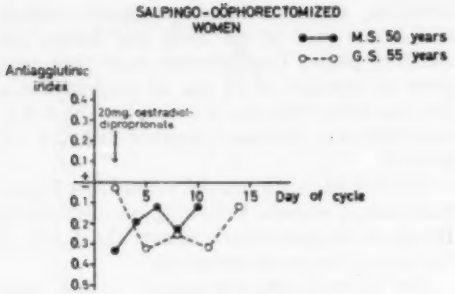

FIG. 11

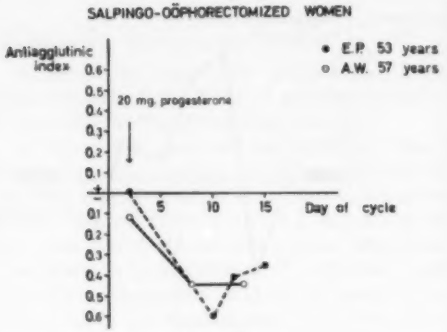

FIG. 12

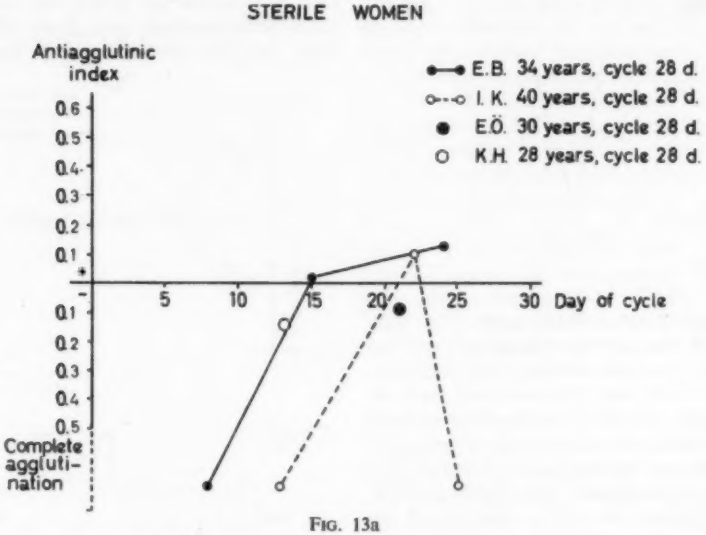
STERILE WOMEN
Antiagglutinic index
E.B. 34 years, cycle 28 d.
I. K. 40 years, cycle 28 d.
E.Ö. 30 years, cycle 28 d.
K.H. 28 years, cycle 28 d.
Day of cycle
Complete agglutination

FIG. 13a

further. Later the A.A.I. increased in all cases and reached positive values. Before the treatment no oestrogens were found in the urine, but simultaneously with the appearance of increasing A.A.I.-values in the cervical mucus an oestrogenic excretion could be demonstrated in the urine. This interesting observation is being further studied by Furuhjelm and Ingelman-Sundberg. If, however, salpingo-oöphorectomy has been performed neither oestrogens nor progesterone can give a positive A.A.I. (Figs. 11, 12).

(6) *Sterility*

In 4 cases of sterility with normal menstruation, normal secretory endometrium, normal hysterosalpingography, and normal sperm analysis the A.A.I. showed interesting values. In the middle of the cycle low or negative values were found (Fig. 13). After the cervical mucus had been reduced with sodium thioglycollate the figures became normal (Fig. 13b), demonstrating that the A.A.F. was present but in the oxidized form, a fact which possibly explains the infertility.

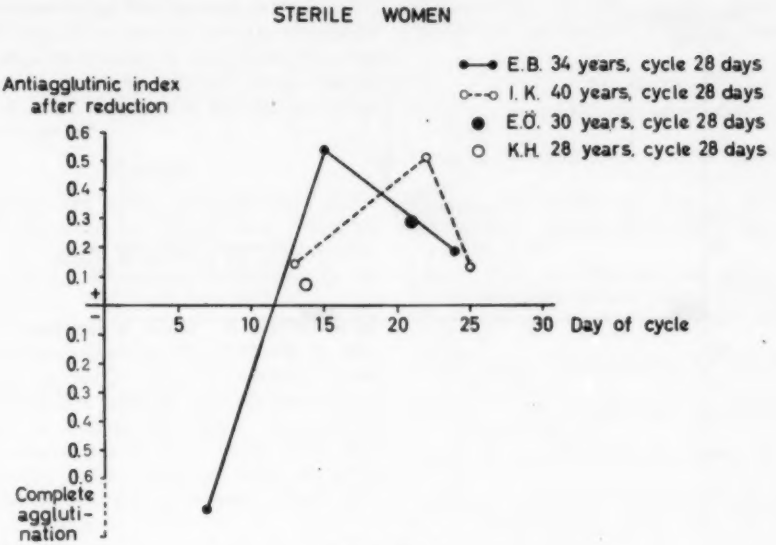

FIG. 13b

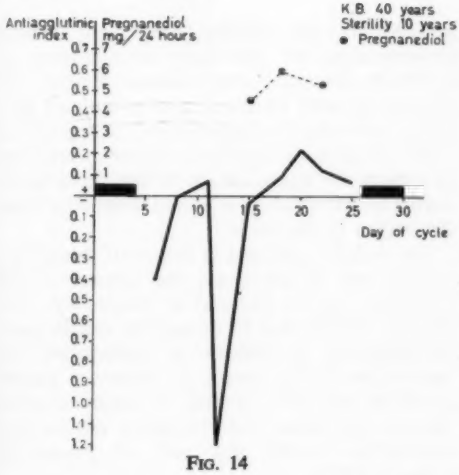

FIG. 14

Another analogous case presented interesting circumstances. As seen from Figure 14 the cervical mucus corresponding to ovulation agglutinated the sperm cells instead of abolishing the agglutination. Unfortunately the cervical mucus was not examined after reduction so we do not know whether the A.A.F. was present but in inactive form at that moment. Before and after ovulation the A.A.I. was positive.

Finally Figure 15 presents a case, 33 years old, who came to treatment for sterility. She had oligomenorrhoea. The temperature curve gave no evidence of ovulation, and the A.A.I. of the cervical mucus was negative on several occasions even after reduction. Following treatment with oestrogen the A.A.I. became positive, and after progesterone she had an artificial menstruation. After that time she had amenorrhoea, climacteric symptoms, increased excretion of gonadotrophins, and the A.A.I. remained negative.

DISCUSSION

This investigation was carried out in order to study whether the sperm anti-agglutinic factor (A.A.F.) described by Lindahl and Kihlström (1952) was present in women, and if it had any interest from a clinical point of view. It has been demonstrated in growing follicles, in the tubes, and in the cervix.

The presence of the A.A.F. in the cervical

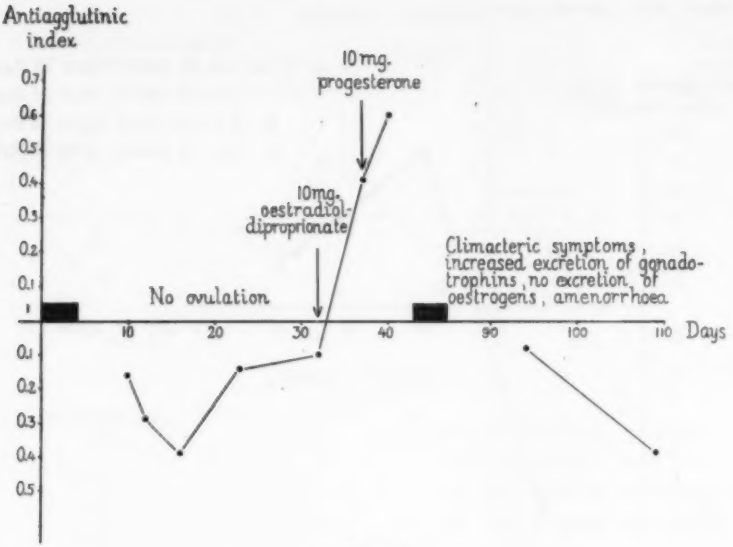

FIG. 15

U.W., 33 years, ovarian insufficiency, oligomenorrhoea.

mucus is secondary as it disappears after salpingectomy. Part of it is probably produced by the mucous membrane of the tubes as it is found in post-menopausal women after oestrogenic stimulation, if the tubes are left. A production by the senile atrophic ovary seems highly improbable. The A.A.F. is also produced by the growing follicle, but disappears from the follicle fluid as soon as corpus luteum formation takes place. As demonstrated in rabbits the A.A.F. of the follicle fluid appears in the tube after ovulation (Lindahl and Nilsson, 1954). This is in agreement with Odeblad's (1954) finding that the follicle fluid is transferred with the egg into the tube at ovulation. Part of the A.A.F. observed in the cervix after ovulation in women may therefore have originated from the ruptured follicle. However, nothing can be said at present about the relative size of the contribution from these two sources. In the rabbit the production of A.A.F. by the mucous membrane of the tubes ceases at ovulation (Lindahl and Nilsson, 1954).

The A.A.F. seems to be of importance for the normal sexual function of the woman. Its presence in the cervical and tubal mucus corresponding to the time of ovulation is probably necessary for normal fertility as cervical as well as tubal mucus without this factor promotes the agglutination of the sperm heads. There is apparently a delicate mechanism to prevent the agglutination of the sperm heads during the penetration of the spermatozoa from the vagina to the ovum.

The A.A.F. is present in the cervix during the middle part of pregnancy but absent in the beginning and at the end of pregnancy. The function of the A.A.F. during the middle part of pregnancy is difficult to understand. Its appearance in the cervix is, however, understandable as there is still a communication between the tubes and the cervix outside the membranes during this part of pregnancy (Thorén, 1955).

The production of the A.A.F. is under hormonal influences. It is stimulated by oestrogens, and seems to be inhibited by progesterone.

Determinations of the A.A.F. may be of importance in cases of sterility, as we have found

patients where it has been present in the inactive oxidized form. This fact can give the possibility of an adequate therapy in such cases. In cases with normal ovulatory cervical mucus lacking the A.A.F. tubal occlusion at the uterine cornua must be suspected.

Summary

In women the sperm anti-agglutinic factor (A.A.F.) described by Lindahl and Kihlström (1952) has been demonstrated in ovarian follicles, in the tubes, and secondarily in the cervical mucus.

The production of A.A.F. is stimulated by oestrogens and seems to be inhibited by progesterone. In some cases of sterility, where hitherto available methods had failed to explain the cause of sterility, the A.A.F. was present only in the inactive oxidized form at the time of ovulation. After treatment with reducting agents the cervical mucus showed normal anti-agglutinic activity.

The investigation has demonstrated that a determination of the A.A.F. ought to be included in the analysis of sterility cases.

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A FLUID RETENTION SYNDROME ASSOCIATED WITH SEVERE ISO-IMMUNIZATION TO THE RHESUS FACTOR

BY

D. T. O'DRISCOLL, M.D., M.A.O.

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SCANT attention has been paid to the maternal complications associated with iso-immunization to the rhesus factor, the bulk of the published work dealing solely with what happens to the infant as a result of this occurrence.

Mention has been made of the more frequent occurrence of toxaemia of pregnancy in these women (Javert, 1942) and more recently, where the foetus dies *in utero* and is retained for some time, the possibility of afibrinogenaemia developing has been recognized.

It is also known that difficulty may arise during the birth of a hydropic infant, which may require evisceration and that repeated stillbirth causes psychological trauma, but there the matter rests.

It is the purpose of this communication to describe a fluid retention syndrome occurring in expectant mothers who carry an infant severely affected by rhesus antibodies. As far as the author is aware this syndrome has not been previously described.

The clinical picture is one of massive oedema. This is especially obvious in the dependent parts of the body, the legs, lower abdomen and sacral pad showing marked pitting on pressure. Characteristically, also, large blebs occur on the abdominal wall involving the striae gravidarum. There was no clinical evidence of oedema in the upper parts of the body in the 3 cases seen to date. This oedema may develop very rapidly in the course of a few days, and disappears within hours of delivery. The infant has been severely affected in all cases: one infant died *in utero* at the 28th week and was already dead when first seen, another patient was delivered at the 32nd week of a huge hydropic infant which required evisceration to overcome obstruction, and the 3rd infant born at term and died within 12 hours despite exchange transfusion. In all cases the placenta was very large, and the liquor amnii was bile-stained.

The condition of the mother is so characteristic that one can be sure that, if the oedema is not cardiac or nephritic, and if the blood pressure and urine are normal, the mother is carrying a severely affected haemolytic infant. There is no rise in blood pressure or albuminuria, unless there is a superimposed pre-eclampsia, and this did not occur in the cases described here.

CASE REPORTS

Case 1. Mrs. M.M., aged 29 years, was first seen on 17th January, 1953. Her last menses was on 10th August, 1952, and her expected date of delivery was 17th April, 1953. She had 5 previous pregnancies. In 1947 she had a spontaneous delivery of a full-time normal healthy infant who was alive and well. In 1948 she had another normal delivery at term; the child was alive and well. In 1949 she had a 12-weeks abortion. In 1950 she had another full-time normal delivery; the child was alive and well and there was a slight post-partum haemorrhage at this birth. In 1951 she was again delivered spontaneously of a full-time healthy infant. None of these children had any evidence of jaundice at or after birth. All the children had been born in a rural practice and no blood investigations had been carried out.

She now complained of breathlessness and faintness. She had had a slight haemorrhagic vaginal discharge on 23rd December, 1952 and again on 6th January, 1953, and again on 15th January, 1953. She was referred for an opinion because of these symptoms.

On examination the patient was noticed to be pale, with a mild icteric tinge. She had some breathlessness on exertion. Her lungs and heart were normal. The uterus was about the size of a 32-weeks pregnancy. The vertex which presented was free. An X-ray of the abdomen was reported on as follows:

"No definite evidence of placenta in the upper segment. The space between the foetal head and the promontory of sacrum is greater than normal. I am suspicious that the placenta is situated posteriorly in the lower segment. The symphysis pubis is very wide. There must have been disruption."

The blood was group O, Rh negative. The haemoglobin was 35 per cent, the colour index 0·64, M.C.V. 70, M.C.H.C. 27 per cent, M.C.H. 18. The platelets and white cells were normal. No immature cells were seen. The urine was albumen-free and the blood pressure was 130/80.

A diagnosis of placenta praevia with a severe degree of anaemia partially due to the vaginal bleeding and partially due to iron deficiency was made, and the patient was admitted to hospital. The patient was treated with intravenous iron and rest. There was no further bleeding. On 16th February, 1953 the haemoglobin had risen to 11·8 g. or 80 per cent. It was noted that the serum had a mild icteric tinge. The patient had now become very oedematous. Her weight on 7th February, 1953 was 13 stones and on 14th February, 1953 she weighed 13 stones 4 pounds. The oedema was very marked in the legs, on the lower abdomen, and over the sacrum. The blood pressure was 130/90 mm. Hg and the urine was albumen-free; it contained a trace of bilirubin but there was no urobilinogen present. The uterus was estimated to be about 32-weeks pregnant. The vertex was presenting. The serum protein was 5·5 mg. per 100 ml., and the albumen/globulin ratio was normal. The prothrombin time was 17 seconds, the thymol turbidity test was positive.

On the 21st February, 1955, the patient went into labour. At this time the blebs on the abdominal wall were very obvious. There was delay in the second stage due to the massive size of the foetal abdomen which required evisceration. Several pints of bile stained fluid were released from the foetal abdominal cavity. A large oedematous placenta was removed.

The oedema cleared rapidly and was gone within 48 hours of delivery. On the 24th February, 1953 the blood count was 4,900,000 red cells with 12·8 g. of haemoglobin or 87 per cent, the M.C.H.C. was 32 per cent and the haemocrit 41 per cent. The serum was still mildly icteric, the thymol turbidity test was negative, the prothrombin time was 17 seconds. The direct Van Den Berg was still positive. The urine contained a trace of bilirubin but no urobilinogen. She made an uneventful recovery.

Case 2 had 13 previous deliveries. Three died of jaundice; the others were alive and well. The first day of her last period was 1st November, 1954. The expected date of delivery was 8th August, 1955. On examination the cardiovascular system was normal. The blood pressure was 130/80. There was a mild oedema of the ankles. The urine was albumen- and sugar-free. The foetus was approximately 32 weeks and presented by the vertex. There was mild hydramnios. The haemoglobin was 60 per cent. She was group O, Rh negative. The indirect Coombs test was negative.

The patient was seen again on 13th July, 1955. The fundus was at a height equivalent to 36 weeks pregnancy. The urine was albumen-free and the blood pressure was 120/80. The patient weighed 15 stones on 24th July, 1954. The foetal heart was present. The patient was next seen on 1st August, 1955 in labour. She was noticed to be grossly oedematous. The oedema involved the legs and the abdominal wall, and the typical bullae were seen involving the striae gravidarum. She was delivered after 2-hours labour of a live-born male infant weighing 7½ pounds. The infant was deeply jaundiced at birth and died after 24 hours despite exchange transfusion. The oedema cleared completely within 24 hours of birth.

This patient has subsequently had an intra-uterine death of a foetus retained for 10 weeks, and developed afibrinogenaemia which necessitated a Caesarean hysterectomy (O'Driscoll and Lavelle, 1955) and concentrated plasma transfusion.

Case 3. This patient was seen for the first time in premature labour on 10th September, 1955. She was 41 years old, and had one previous pregnancy in 1939. She was then delivered of a normal healthy infant, who was still alive and well. She had had no treatment for her failure to conceive. Her last menses was on 10th April, 1955. She had had no prenatal care and had felt well through her pregnancy. She had not felt movement for 2–3 days before admission.

The patient was grossly oedematous, similar to the two previous cases, and the bullae were again seen on the abdominal wall. The blood pressure was within normal limits and the urine was free from albumen. The uterus corresponded to a 30- to 32-weeks pregnancy. No foetal heart was heard.

Within a few hours of commencement of labour the patient was delivered of a hydrops infant with a typical large oedematous placenta.

Six hours after birth her weight was 10 stones 4 pounds and 48 hours later this had decreased to 9 stones 2 pounds a loss of 16 pounds. Her fluid intake for the three days after delivery was 99 ounces and the amount of urine passed was 116 ounces.

Unfortunately a sample of the fluid in the blebs was not taken for analysis. But they had completely disappeared within 6 hours of birth.

The maternal blood was Rh negative and the indirect Coombs test was positive.

The first and third cases are unusual in that a very severely affected infant was born without any previous evidence of maternal sensitization.

Discussion

The clinical picture described in these 3 cases is one of gross oedema of the lower parts of the body with the formation of blebs on the abdominal wall. The usual causes of oedema, such as heart failure, nephritis and pre-eclampsia, are absent.

The cause of this gross oedema is still a matter for conjecture. The condition is unlikely to be purely mechanical; many other conditions in which large pelvic swellings occur are not accompanied by this amount of oedema.

The causes of fluid retention are complex, and several factors could be involved in the type of case here described, but the most likely causes are toxins produced by a hydrops infant and acting on the maternal capillary endothelium and renal parenchyma, and perhaps on the adrenal gland. The condition may also have an allergic basis, the swelling being akin to giant urticaria. It was interesting to note that the second patient developed afibrinogenaemia in her next pregnancy. The mother to some degree mirrors the oedema of the infant.

Summary

A fluid retention syndrome occurring as a complication of iso-immunization of the mother to the Rh antigen is described. The syndrome is characterized by a massive dependent oedema with marked pitting on pressure. Large blebs involving the striae gravidarium are also usually present.

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VAGINAL CYTOLOGY IN CANCER OF THE CERVIX

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IN a previous communication (Liu, 1955) the vaginal cornification assessed by the vaginal smear method was found to be increased in patients with uterine cancer as compared with patients of comparable age but without cancer. This report is to present the findings in another group of 316 patients with carcinoma of the cervix who showed a similar increase of vaginal cornification when compared with a group of 300 patients without cancer. In addition, there was found also an increased number of basal cells in the cancer group.

MATERIAL AND METHOD

The material was taken from patients treated by the Newcastle Regional Cancer Organization. In the period between January, 1952 and July, 1955, a total of 416 new patients with primary carcinoma of the cervix was seen. Three hundred and sixteen patients had satisfactory vaginal smears taken before their treatment and these smears were evaluated as to the proportions of their cellular contents. Another group of 300 smears from patients of comparable age but without cancer was used for comparison. These latter were obtained from smears taken at gynaecological out-patients from patients who were known not to have cancer, prolapse, nor any gross endocrine disturbance. It is regretted that it was impossible to obtain a similar number of smears from healthy women but it is hoped that such will be available in the course of time.

The proportions of cornified, pre-cornified and basal cells were obtained in each smear as described previously (Liu, 1955). The amount of each cell type was grouped, according to its level, under one of the four arbitrary grades of minimum 0–10 per cent, moderate 11–30 per cent, advanced 31–60 per cent, and marked 61 per cent or more.

RESULTS

The ages of 316 cases with cancer of the cervix varied from 26 to 77 with peak incidence between 50 and 59. The age distribution of the non-cancer group was similar (Fig. 1).

(1) Comparison of cornified cells between patients with and without carcinoma of the cervix.

The amount of cornified cells present in the vaginal smears varied greatly from one individual to another of a similar age, and the range of variation between one cancer patient to another was just as great as that among patients without cancer. However, when the two groups of patients were compared as a whole, there were some differences which are shown in Fig. 2.

Among the 316 patients with carcinoma of the cervix: 81 or 26 per cent of them had a minimum amount of cornification, 81 or 26 per cent had moderate, 87 or 27 per cent had advanced, and 67 or 21 per cent marked cornification. On the other hand, among the 300 patients without cancer: 167 or 55 per cent had minimum, 61 or 20 per cent had moderate, 44 or 14 per cent advanced and 28 or 9 per cent marked cornification. This comparison is in accordance with what was presented previously.

(2) Comparison of vaginal basal cells between patients with and without carcinoma of the cervix.

* This work has been carried out on a grant to one of us from the trustees of the will of the late Mrs. M. O. Gordon to whom we wish to express our thanks and acknowledgments.

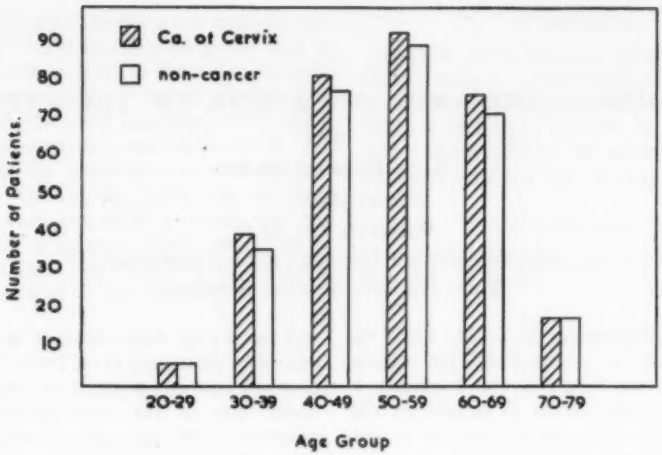

FIG. 1
Age distribution of 316 cases of carcinoma of the cervix and 300 cases without cancer.

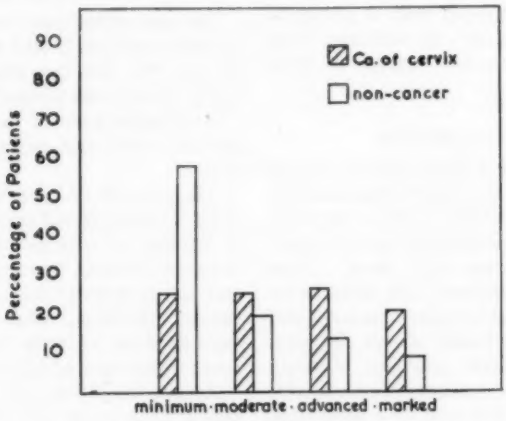

FIG. 2
Comparison of vaginal cornification between patients with and without carcinoma of the cervix.

The amount of basal cells in the vaginal smears also varied from one individual to another of a similar age with and without cancer of the cervix. When the two groups of patients were compared it was found that in the group with carcinoma of the cervix more patients showed higher basal cell count than in the group without cancer (Fig. 3).

Among the 316 patients with carcinoma of the cervix: 150 or 47 per cent of them had a minimum amount of basal cells, 66 or 20 per cent had moderate, 52 or 16 per cent advanced, and 48 or 15 per cent a marked degree of basal cells. In the 300 patients without cancer: 228 or 76 per cent had minimum, 30 or 10 per cent moderate, 28 or 9 per cent advanced and 14

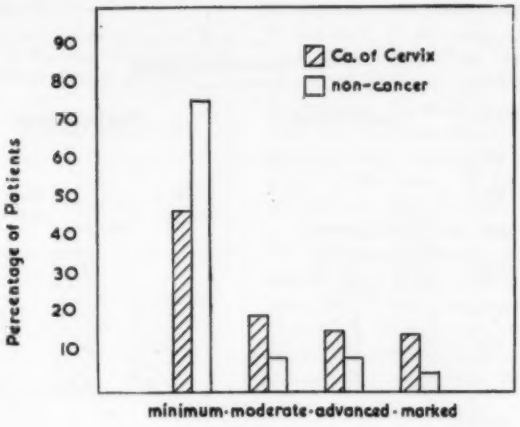

FIG. 3

Comparison of vaginal basal cells between patients with and without carcinoma of the cervix.

or 5 per cent marked degree of basal cells.

(3) Comparison of the vaginal cornification and basal cells between patients with and without carcinoma of the cervix.

The data, so far, show that there are more patients in the cancer group who have a higher degree of vaginal cornification than in the non-cancer group; furthermore, there are more patients in the cancer group with higher degrees of basal cells. It became necessary to see which patients were those having increased cornified cells and which having increased basal cells. Scattergrams were made separately for the two groups of patients and the level of cornified cells (ordinate) and the level of basal cells (abscissa) were plotted simultaneously for each of the 616 patients.

It was seen that, in the group of patients without cancer, the majority of those who had moderate to marked cornification had only a minimum degree of basal cells. In many, the smears were primarily pre-cornified with few or no cornified and/or basal cells. On the other hand, in the cancer group there were more patients with moderate and marked cornification who also had a moderate amount of basal cells present. Table I shows that, in 316 cancer patients, 94 or 30 per cent of them had both cornified and basal cells at moderate levels (or above), while in 300 patients without cancer only 19 or 6 per cent showed such a picture. Thus it was more common among patients with cancer of the cervix to have both cornified and basal cells increased simultaneously.

TABLE I

Comparison of Vaginal Cornification and Basal Cells Between Patients With and Without Carcinoma of the Cervix

	No. of Patients having Moderate Amount of Both Cornified and Basal Cells
Cancer—316	94 (30 per cent)
Non-cancer—300	19 (6 per cent)

(4) Comparison of pre-menopausal and post-menopausal patients with and without carcinoma of the cervix.

In order to see if the menopause played any role in the cytologic difference between patients with and without cancer, especially in regard to the simultaneous increase of cornified and basal cells in the cancer group, the smears from patients before and after the menopause were

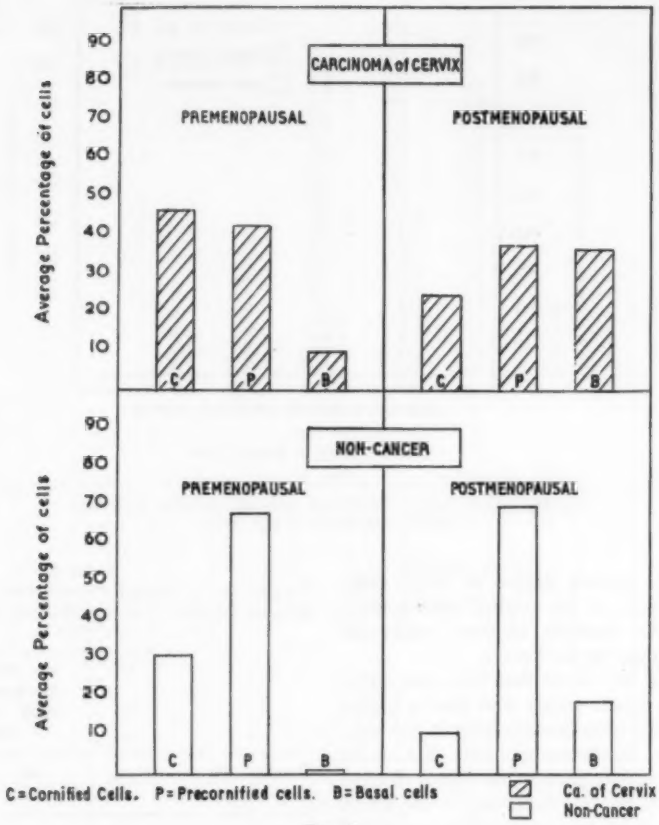

FIG. 4

Comparison of average percentages of cornified, pre-cornified and basal cells in the vaginal smears of pre- and post-menopausal patients with and without carcinoma of the cervix.

separated. In 316 cancer patients: 135 were pre-menopausal and 181 were post-menopausal. Among 300 patients without cancer 132 were pre-menopausal and 168 were post-menopausal.

For each of the four groups of patients—pre-menopausal and post-menopausal patients with and without carcinoma of the cervix—a scatter-gram was made so that the levels of cornified and basal cells were plotted simultaneously. It was noted that both pre- and post-menopausal cancer groups have more patients showing a higher number of cornified as well as a higher number of basal cells than the two groups of patients without cancer. The increase was at the expense of the pre-cornified cells.

This point was further analyzed by comparing the average percentage of each cell type in the four groups of patients. The percentage figures of cornified cells of all the patients in the same group were added and a mean was taken as the average level of cornified cells of this group. This was repeated with pre-cornified and basal cells. The results are shown in Table II and Fig. 4.

In the cancer group, the average percentages of cornified, pre-cornified and basal cells of pre-

TABLE II

Average Percentage of Cornified, Pre-cornified and Basal Cells in Vaginal Smears of Pre- and Post-menopausa Patients With and Without Cancer of Cervix

	Average Amount of		
	Cornified (per cent)	Pre-cornified (per cent)	Basal (per cent)
Cancer:			
Pre-menopausal ..	47	43	10
Post-menopausal ..	25	38	37
Non-cancer:			
Pre-menopausal ..	31	68	1
Post-menopausal ..	11	70	19

menopausal and post-menopausal patients were: 47 per cent, 43 per cent, 10 per cent, and 25 per cent, 38 per cent, 37 per cent, respectively. In the group of patients without cancer the average percentages of cornified, pre-cornified and basal cells for pre-menopausal and post-menopausal patients were 31 per cent, 68 per cent, 1 per cent, and 11 per cent, 70 per cent, 19 per cent, respectively. This showed that the average levels of pre-cornified cells between pre-menopausal and post-menopausal cancer patients were very similar, and those between the two groups of patients without cancer were also close. Nevertheless, in cancer patients both cornified and basal cells simultaneously increased, resulting in a lowered average level of pre-cornified cells.

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THE VALUE OF CYTOLOGY IN THE EARLY DIAGNOSIS OF CARCINOMA OF CERVIX

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A CONSIDERABLE volume of literature has appeared on the subject of the cytological diagnosis of neoplastic disease since Papanicolaou and Traut's classical paper in 1941. Earlier writers, notably Dudgeon and Patrick (1927) had used wet film smears in the examination of neoplastic tissue and Wrigley (1932) and Bowes and Barrett (1935) had applied the method to lesions of the female genital tract. Following Papanicolaou's paper the taking of smears from the posterior fornix and the cervix was widely adopted in North America. In Britain the method has been less widely used and it was with a view to examining its practical value in the gynaecological department of a general teaching hospital that the present investigation was carried out.

METHOD AND MATERIAL

The patients investigated were those attending the gynaecological out-patient department or admitted to gynaecological wards of King's College Hospital during the period 1st December, 1952 to 31st March, 1955. During the first 9 months from 1st December, 1952 until 31st August, 1953 cytological investigations were undertaken on all patients over the age of 30 who had symptoms which might have been caused by cancer of the cervix. In the 18-months period 1st September, 1953 to 31st March, 1955 *all* patients over the age of 30 attending the gynaecological department were investigated.

Cytological samples were taken from each patient by means of the wooden spatula designed by Ayre (1946). A sample of secretion from the posterior fornix and a scraping from the surface of the cervix were smeared on to separate glass slides and examined.

STAINING AND PREPARATION OF SMEARS

Immediate fixation of the smears is essential if satisfactory nuclear definition is to be obtained and in this series the smears were fixed in Schaudinn's solution. After 10 minutes in the fixative the smear is transferred to an alcoholic solution of iodine prior to staining. Although the optimum time for fixation is 10 minutes it was found convenient when dealing with large numbers of smears in the out-patient clinic to leave them in the fixative until the end of the clinic, transferring them to iodine solution on arrival in the laboratory. No loss of nuclear definition seemed to result from this alternative procedure. After washing, the smears were stained with Mayer's Haemalum and Eosin, dehydrated and cleared with alcohol and xylol and finally mounted under a cover slip with Canada balsam. This method, first described by Dudgeon and brought to the writer's notice by Dr. J. Bamforth, is very much simpler and easier to carry out than the complicated method described by Papanicolaou (1942) and the time spent in preparing the smears is correspondingly reduced. The differentiation of the cytoplasm of epithelial squames and basal cells is not so obvious but this does not seem to be a disadvantage in the detection of malignant cells, especially as the nuclear definition is excellent. A uniformity in the staining of smears is more readily obtained than with the Papanicolaou stains and furthermore smears can be easily compared with the routine Haematoxylin and Eosin pathological section, an advantage in deciding the origin of doubtful cells in a patient on whom a biopsy has also been performed.

Interpretation of the smears was carried out

by a laboratory technician and a medically trained gynaecological research assistant. Where there was doubt about the interpretation of a smear it was referred to a specialist cytologist (Dr. J. Bamforth) for a further opinion. Repeat smears were taken where the initial smears were questionable and if these continued to show abnormal cells a cervical biopsy was recommended.

Results

The results obtained refer only to carcinoma of the cervix. The cytological diagnosis of carcinoma of the corpus uteri is less reliable in most hands and is probably less valuable in that most patients with this condition present with symptoms which will in any case require a diagnostic curettage. Carcinoma of the corpus uteri was in fact diagnosed correctly in 16 cases but there was a high incidence of false negative smears (5 cases), and in no case did the cytological diagnosis precede the clinical suspicion and hence full investigation.

Table I

	Period I 1.12.52 to 31.8.53	Period II 1.9.53 to 31.3.55	Totals
Patients examined ..	256	799	1,055
Positive smears:			
Invasive carcinoma of cervix	14	29	43
Carcinoma *in situ* ..	1	1	2
No carcinomatous lesion demonstrated	2	2	4
Negative and questionable smears	239	767	1,006

It will be seen from Tables I and II that in 3 cases with positive smears the diagnosis of carcinoma of the cervix was unsuspected at the time of the patient's initial visit to hospital when the first smears were taken. Of these 3 cases 1 was an invasive carcinoma and 2 were *in situ* lesions. The criteria upon which the latter lesion is diagnosed vary considerably from pathologist to pathologist and in this series only those satisfying the strict criteria laid down by Novak (1950) were placed in this category. The incidence of *in situ* lesions as compared with invasive lesions is 4·4 per cent. In the Mayo Clinic series reported by Pratt (1954) the comparable figure is 24·6 per cent, a much more substantial proportion of the total number of lesions.

In 4 cases smears were interpreted as being positive for malignant cells where no corresponding lesion was subsequently demonstrated. (A false positive incidence of 8·1 per cent.) In all 4 the uterus was removed for associated non-malignant pathology and serial section of the entire uterus was performed. In 2 cases, lesions which were presumably the origin of the abnormal cells were discovered, but in the remaining 2 cases, both associated with prolapse, no pathological lesion was demonstrable. Negative smears in the presence of an invasive carcinoma of the cervix were found in 2 patients in the present series. In 1 case the lesion was suspected clinically and diagnosed on biopsy, the negative smear being ignored in the face of a clinical suspicion. The second false negative smear occurred in a patient with an adenocarcinoma of the cervix and the lesion was not diagnosed until 6 months after the patient's first visit to hospital. Ayre has claimed that a negative scrape smear is conclusive evidence of the absence of cancer but the above 2 cases whose initial smears remained negative even on retrospective examination emphasize the now generally accepted view that this is not the case.

None of the remaining 967 patients with negative smears have developed cervical cancer thus far and can be regarded as true negatives although the follow up period is short and some may possibly do so.

Thirty-seven patients in this series gave initial smears whose interpretation was questionable. In 4, thought to be suspicious of cancer, a carcinoma of the cervix was diagnosed on biopsy. Nine patients had at least 2 negative repeat smears and 19 patients had a negative biopsy in addition to negative repeat smears. In 5 cases the follow up was inadequate.

The results shown in Table III indicate that there is no significant difference in the number of positive results obtained by the cervical scrape smear and the "vaginal" smear prepared from a drop of secretion taken from the posterior fornix. In 2 patients (4·8 per cent) a positive result would have been missed if only one smear

TABLE II

Positive Smears	
Total positive smears	49
Invasive Carcinoma—43 cases	
Clinically diagnosed or suspect when first smear taken	41
Clinically suspect when first smear taken, initial biopsy negative	1
Clinically unsuspected when first smear taken	1
Carcinoma *in situ*—2 cases	
Clinically diagnosed or suspect when first smear taken	0
Clinically unsuspected when first smear taken	2
No Carcinomatous lesion demonstrated—(False Positive Smears)—4 cases	
Squamous metaplasia and metropathia haemorrhagica—Hysterectomy. Serial section	1
Benign adenomatous polyp and fibroids—Hysterectomy. Serial section	1
No pathological lesion found after serial section of cervix and corpus uteri	2
Negative and Questionable Smears	
Total Negative Smears	969
No malignant cervical lesion diagnosed subsequently	967
Invasive carcinoma of cervix diagnosed subsequently (False negative smears)	2
Total Questionable Smears	37
Invasive carcinoma of cervix diagnosed subsequently	3
In situ carcinoma of cervix diagnosed subsequently	1
Repeat smears negative	9
Repeat smears and cervical biopsy negative	19
Inadequate follow-up	5

TABLE III

Comparison of Vaginal and Cervical Positive Smears

	Invasive Carcinoma	Carcinoma *in situ*	No Carcinomatous Lesion
Total number of cases	43	2	4
Both smears positive	37	2	4
Cervical smears alone positive	1	0	0
Cervical smear positive, vaginal smear not taken or unsatisfactory	4	0	0
Vaginal smear alone positive	1	0	0

had been taken from the patient. As against this however is the fact that the amount of time spent scanning smears is doubled and in what is already a time-consuming process this hardly seems justified. Both smears were positive in the 4 cases where no carcinoma was subsequently found. In practice it has been found that the cervix which bleeds readily on contact yields a cervical smear somewhat obscured by the presence of large numbers of red cells and in these patients a vaginal smear gives a better cytological picture. On the other hand, where profuse infective vaginal discharge is present the vaginal smear is obscured by the presence of large numbers of pus cells with darkly staining nuclei. In these patients the scrape smear taken directly from the cervix is of greater value.

DISCUSSION OF RESULTS

The 3 patients in whom a clinically unsuspected lesion was diagnosed cytologically represent the positive result of the present

investigation. Two of these patients had a carcinoma *in situ* and 1 had an invasive carcinoma. Most writers accept that the former lesion represents the earliest stage in the life of an invasive carcinoma where epithelial hyperplasia has started but invasion has not occurred (Peel, 1950). The discrepancy between the incidence of the *in situ* lesion in different series of cases must be due in part, at least, to different pathological criteria in making this diagnosis. It seems probable, as pointed out by Novak (1950), that in some centres the distinction is not drawn between basal cell hyperactivity and true carcinoma *in situ*.

The incidence of surprise positive smears in the series is 1 in every 351·6 patients examined and since 2 smears were taken from each patient 703 had to be scanned for each unsuspected positive result. Even though the simple staining technique took up a minimum of time in the preparation of the smears this represents a considerable expenditure of effort and, allowing an average of 12 minutes for each smear, means that 140 hours were spent scanning negative smears before an unexpected positive result was obtained. In 3 patients however a carcinoma was diagnosed at the earliest possible time when therapeutic measures should be highly successful. From a consideration of the numbers of unsuspected lesions detected and the numbers of patients over 30 years of age attending the gynaecological department it seems likely that about 0·3 per cent of such patients will have a cervical cancer which can only be detected by cytological examination. The large majority of surprise positive smears will occur in the *in situ* group.

It is significant that of the 43 cases of invasive carcinoma 42 or 97·7 per cent were diagnosed or suspected at their first visit to the department. Thus the large majority of lesions are lost to the hospital cytologist in that once the suspicion is raised urgent and complete biopsy as advocated by Anderson (1950) is indicated and cytological studies in these patients are no more than confirmatory. Way (1951) showed that in a series of 540 patients with invasive carcinoma of the cervix only 15 required biopsy to confirm the diagnosis which was usually obvious clinically. Failing earlier cytological access to the patient by the taking of smears in the practitioner's surgery or the mass screening of the female population, the gynaecologist must continue to rely in the main upon the patient to report her symptoms early and for her family doctor to suspect the presence of cancer with equal alacrity.

The most difficult problem which faces the cytologist from the diagnostic point of view is the questionable or doubtful smear, where differentiation between malignant cells and atypical non-malignant cells may be extremely difficult. Repeat smears are essential in these patients and where doubt persists as to the nature of the atypical cells a ring biopsy is indicated. In the present series, 19 patients with questionable smears were submitted to biopsy without cancer being found. Of these 19, 3 showed hyperplasia of the squamous cervical epithelium, 2 showed metropathia and in 5 an adenomatous polyp was present. The latter lesion seems particularly liable to produce atypical cells and, especially when some degree of infection is present, they may be mistaken for cancer cells. Early recourse to biopsy is the best way of elucidating the problem.

Conclusion

The efficiency of the cytological method in the diagnosis of carcinoma of the cervix has been amply confirmed in the present series and although it is very time-consuming it is the only way in which the very small percentage of lesions may be diagnosed at the time of the patient's first visit to the gynaecological department. At the present time the vast majority of patients with invasive cancers present with clinically detectable lesions and for these patients cytology has little to offer except to confirm a clinical suspicion or occasionally to call attention to the need for a further biopsy where the initial specimen does not confirm a clinical suspicion of malignancy.

Summary

One thousand and fifty-five patients attending the gynaecological department have been examined by means of cervical and vaginal smears. A simple staining technique is described and the results are analyzed and discussed.

I am deeply indebted to Dr. J. Bamforth without whose assistance this study could not have been undertaken, to Mr. J. H. Peel and Mr. S. G. Clayton for their advice and encouragement and to Professor H. A. Magnus for his help in interpreting the histological sections. Preparation and screening of many of the smears was carried out by Mr. S. Hardy.

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OTTO PELVIS

A Report of Two Cases Associated with Labour

BY

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REPORTS on the occurrence of labour in women with intrapelvic protrusion of the acetabula are rare. This is probably due to the fact that it was formerly thought that this abnormality only occurred in middle-aged persons. In view of the rarity of the condition it is not surprising that no mention of this abnormality of pelvic architecture is made in the usual classification of pelvic types in obstetrical literature or standard obstetrical works.

Within the past 3½ years 2 patients presented themselves to our unit with the abnormal features associated with this pelvic abnormality.

Definition. The "Otto" pelvis may be defined as "an affection of the hip joint characterized anatomically by deepening of the acetabulum with mesial displacement of the inner wall" (Hertzler, 1922). The condition has also been described by the following terms: intrapelvic protrusion of the acetabulum; protrusio acetabuli; acetubular bulging; arthrokatadysis; Chrobak pelvis; coxarthrolisthesisbecken and osteoarthritic protrusion of the acetabulum.

Historical and Literature Review. A. W. Otto (1824) first described this pelvic abnormality from a specimen in an anatomical museum and termed it "a pelvis with globular extensive acetabula". His son, A. C. Otto (1845), published a lithograph of the pelvis. The first case described in the English literature was that of Hale-White (1883). Prior to 1921 most articles on the subject appeared in the German literature and up to that year only 31 cases were collected from the literature (Valentin and Müller, 1921). Hertzler (1922) was the first to write on this subject in the American literature. Since that time papers have appeared devoted mostly to reports of cases. Reviews of the literature were presented by Henschen (1910), Benda (1926–1927), Pomeranz (1932) and Brentrup (1942). Sloane and Sloane (1937) collected 106 cases reported in the literature up to that time. The largest series was reported by Scandalis, Ghormley and Dockerty (1951) who analyzed 50 cases seen at the Mayo clinic between the years 1908–1947. They also collected a further 236 cases from the literature. Cases associated with pregnancy and labour were reported by Campbell (1943) and Petersen (1948).

Aetiology. The cause of the condition remains obscure. Otto (1824) regarded the condition as a manifestation of abnormal gout. Eppinger (1903) considered a disturbance of growth affecting the triradiate cartilage to be the responsible agent. Schaap (1934) believed the condition to be due to a congenital deformity of the acetabulum. Rechtman (1936) believed the cause to be an overgrowth of some element in the development of the acetabulum resulting in a congenitally deep acetabulum. Scandalis *et al.* (1951) in reviewing the literature were able to find 31 causes suggested for the condition. The most frequently mentioned as the responsible factor were the following: osteoarthritis deformans, tabes dorsalis, localized osteomalacia or weakening of the acetabulum, inflammation, echinococcus disease, endocrine factors, congenital defects, trauma and gonorrhoea. Henschen (1910) was the first to suggest that the disease may be caused by more than one process.

Classification. Several classifications of Otto pelvis may be found in the literature. Pomeranz (1932) divided his cases into acute and chronic types, regarding the Otto pelvis as "an atypical but essentially non-specific arthritis of the hip joint". Golding (1934) divided such cases into 3 groups: (*a*) Caused by growth disturbances; (*b*) rheumatic group (i) specific (gonococcal)

infections, (ii) non-specific infections, (iii) metabolic arthritides; (*c*) group including many varieties due to gross destructive disease. Scandalis *et al.* (1951) grouped their cases according to Diez's (1939) classification into primary (of unknown aetiology) and secondary (of known aetiology). Of their 50 cases, 41 were of the primary variety and 9 cases of the secondary variety, the causative factors in the latter group being fractures (5 cases), septic arthritis (2 cases), rheumatoid arthritis (1 case) and metastatic hypernephroma (1 case).

Clinical features. The condition is usually found in the middle-aged, but the younger age groups, even infants and young children, are not exempt from the disease, as was shown by Overgaard (1935) and Brailsford (1953). It is more common in females than in males. In the 41 cases reported from the Mayo clinic 85 per cent were females and 15 per cent males, the condition being bilateral in 40 cases (Scandalis *et al.*, 1951). Analyzing 79 cases, Pomeranz (1932) found that 47 occurred in females, being bilateral in 29 cases of the total number. Shortening of the limb may occur should the condition be unilateral. A number of cases has been reported in which the hip joint affection presented as a familial disability (Campbell, 1943). Marked lumbar lordosis associated with the condition has been described by Thoroughman (1945). Pain in the hip joints or thighs with limitation of all movements are the characteristic features. In the Mayo clinic series 36 cases complained of pain in these regions as their chief complaint; 5 cases had defective hip movement as the main complaint (Scandalis *et al.*, 1951). Cases with no complaints have been described (Brailsford, 1953; Thoroughman, 1945). Protrusion of the acetabula can usually be felt on vaginal or rectal examination, and even occasionally on abdominal examination (Thoroughman, 1945). Gilmour (1939) pointed out that the bilateral deformity is associated with an increase in the intercristal diameter and a reduction in the bitrochanteric and intertuberous diameters.

Radiological features. These have been well described by Doub (1929) and Brailsford (1953). The head of the femur, which may have a slightly elongated appearance, is typically intact and is deeply buried in the acetabulum. In the younger age groups Brailsford (1953) has described Perthes' disease of the femoral head in cases with protrusio acetabuli, but he stated that the Perthes' disease should be regarded as an associated condition. The changes in the acetabulum are the most striking. There is thinning of the medial and inferior walls with a dome-shaped protrusion of this into the pelvic cavity. Considerable osteosclerosis may be seen. Osteophytes often project outward at the junction of the head and neck, and some degree of coxa vara may be present. The head of the femur being deeply buried in the acetabulum, it follows that the greater trochanter is closer to the ilium. This, and the presence of osteophytes may effectively limit movement of the joint. Scandalis *et al.* (1951) have graded the amount of intrapelvic protrusion of the acetabulum into 4 grades, depending on the severity, from the mildest to the most severe degree. In their series of 41 cases of primary protrusion 18 presented a mild degree, 17 moderate, 3 moderately pronounced and 1 very pronounced.

Treatment. Relatively little has been mentioned in the literature regarding the best treatment for the condition. Conservative therapy includes the use of traction, physiotherapy, braces and analgesic agents. Surgical treatment includes osteotomy, acetabuloplasty (Smith-Petersen, 1936), or perhaps preferably arthroplasty employing a vitallium cap (Berg, 1940).

Case Reports

Case 1. N.M., a Xosa female, aged 34 and gravida-6 attended the antenatal clinic at the Somerset Hospital for the first time on the 21st May, 1951. She could give no information regarding the date of her last menstrual period nor any relevant history about her previous health. She stated that she had 5 previous normal deliveries but could give the date of only one, in 1948, this being her only living child. Previous to this confinement, which occurred in the Transkei (a Native reserve), she had 2 normal deliveries, both infants being stillborn. Since 1948 she had 2 further deliveries, the one infant having died after a few days and the other having been stillborn. Both the latter confinements occurred in her home in Cape Town. No history could be obtained about the nature of her labours nor about the weights of her babies.

On examination she was found to be of short stature (height not recorded) and showing a marked lumbar lordosis. She weighed 126 pounds. Her blood pressure was 110/70 and the urinary examination revealed no

abnormality. The foetus was presenting by the vertex in the L.O.A. position, the presenting part being mobile. The foetal heart was regular at 134 per minute. She was judged to be 34 weeks pregnant. Vaginal examination revealed an android type of pelvis with a markedly contracted outlet. The Wassermann reaction was negative and the blood rhesus positive. An X-ray pelvimetry was arranged but she failed to attend until 2 months later when she was admitted, having been in labour for 14½ hours.

On examination her general condition was good, the blood pressure was 110/75, pulse rate 96 per minute and urine normal. Abdominal examination revealed a vertex presentation, R.O.A. position, foetal heart rate regular at 130 per minute. The presenting part was still mobile, the membranes intact and the cervix 3 fingers dilated. She was having weak and irregular contractions. An emergency X-ray pelvimetry was done and when the obstetrician saw her 2 hours after admission a Caesarean section was decided upon. However, 20 minutes later the membranes ruptured spontaneously and she started bearing down forcibly. Ten minutes later the foetal heart became irregular and slow and 15 minutes later she gave birth normally (R.O.A.). The baby was very limp at birth and made no attempt at respiration. He died 10 minutes later despite resuscitative measures. The baby weighed 7 pounds 3¾ ounces. The total duration of labour was 17½ hours.

X-ray of pelvis (Figs. 1 and 2). These show bilateral intrapelvic protrusion of the acetabula, as well as the android configuration of the pelvic inlet. The outlet was markedly contracted with a subpubic angle of 55 degrees and an intertuberous diameter of 6·2 cm.

Post-mortem examination of the baby revealed bilateral tentorial tears with massive intracranial haemorrhage.

No note was made of any defect in hip movements in the patient and we have unfortunately been unable to contact her again for further examination.

Case 2. E.B., a Xosa female, aged 17 and primigravida, attended the antenatal clinic at the Somerset Hospital regularly from 19th August, 1954. Her last menstrual period occurred at the end of January and her expected date of delivery was in the beginning of November, 1954. The Wassermann reaction was negative and the blood rhesus positive. Nothing abnormal was noted during her antenatal visits until her 38th week when it was noted that the vertex, presenting in the L.O.T. position, was still mobile. Vaginal examination revealed general contracture of the pelvic brim and bilateral protrusio acetabuli. X-ray of the pelvis confirmed these findings (Figs. 3 and 4). She gave no history of injury or any other disease which may have contributed to this abnormality. She did not complain of any pain in her hip joints and examination revealed a normal range of movement in both joints.

She was admitted to the obstetrical wards on 13th November, 1954 having been in labour for 4½ hours. Her general condition was good, the blood pressure was 120/80, pulse rate 84 per minute, and the urine normal. The vertex was presenting in the L.O.T. position with the presenting part still mobile above the pelvic brim. The foetal heart rate was regular at 140 per minute. She was having irregular contractions at 5–10 minute intervals. Vaginal examination revealed the cervix to be 1½ fingers dilated and the membranes to be intact. She was sedated with bromide and chloral hydrate. After 18½ hours of labour her contractions had become stronger and were now recurring regularly at 5 minute intervals and lasting 40 seconds. Her pulse rate was 96 per minute and the foetal heart rate regular at 140 per minute. The presenting part was still mobile. Twenty-two hours after the onset of labour the findings were still the same except that the cervix had dilated to 3 fingers. She was sedated with morphine. After 31 hours of labour the presenting part was entering the brim of the pelvis and the cervix was 4-fingers dilated. Her contractions at this stage were strong, occurring every 4 minutes and lasting 65 seconds. She was given pethidine and 4 hours later the cervix was fully dilated and effaced. Her pulse rate was 108 per minute and the foetal heart rate regular at 150 per minute. She began to bear down and after a second stage lasting 1 hour an episiotomy was performed. A live male infant weighing 6 pounds 5 ounces was delivered (L.O.A.). The foetal skull showed marked moulding. The third stage was completed in 15 minutes, the total duration of labour having been 36½ hours.

Discussion

By virtue of its disturbance of normal pelvic architecture, intrapelvic protrusion of the acetabula may adversely affect the course of labour. This abnormality causes a reduction in the transverse diameters of the cavity and outlet of the pelvis (Gilmour, 1939) and should therefore be classified amongst the more usually accepted causes of transverse contraction of the pelvis, such as the kyphotic pelvis, the rare Robert's pelvis and the osteomalacic pelvis. The increased lumbar lordosis, which may be associated with the condition (Thoroughman, 1945), was present in Case 1. This may cause an increase in pelvic inclination and so contribute to the failure of the presenting part to engage.

Case 1 demonstrates the fact that with good uterine contractions, fortitude on the part of the mother and extreme moulding of the foetal skull, a marked diminution of available space in the bony pelvis can be overcome. It is clear that this unfortunate woman should not have been

allowed to go into labour but should have had an elective Caesarean section at term. The mere fact that she had been able to deliver 6 babies naturally through such an obviously contracted pelvis, fills one with wonder and admiration at what nature can accomplish in the face of obstacles to natural childbirth. That this tragic obstetrical history need not always be forthcoming in patients afflicted with this pelvic abnormality is shown by the cases of Campbell (1943) and Petersen (1948), as well as by the successful outcome of labour in Case 2. Campbell's (1943) case was that of a primigravida aged 26, who at the age of 15 had a fall from a bicycle. She was admitted to a hospital 3 months after the accident for treatment of painful hips and during the ensuing 26 months was treated first by plaster of Paris immobilization and later by caliper irons. Since that time she had pain and stiffness in both hip joints. During her antenatal visits it was noted that she had marked limitation of both hip joint movements and vaginal examination revealed bilateral protrusio acetabuli, which was confirmed by X-rays. At 34 weeks the foetal head was engaged and at term she went into labour spontaneously, and was delivered normally of a live baby who weighed 7 pounds 4 ounces after only 4½ hours of labour. Petersen's (1948) case was also that of a primigravida aged 32 who was admitted to their hospital 36 hours after labour had started. At that stage the foetal head was not quite engaged in the pelvis and she was having an inco-ordinate type of uterine action. After stimulation with thymophysin a live baby weighing 7 pounds 9 ounces was delivered under chloroform anaesthesia. The total duration of labour was 45 hours. There were pressure marks on both sides of the foetal skull and X-rays of the pelvis showed typical acetabular protrusion. This patient also had restriction of her hip joint movements, but no pain.

The possibility that acetabular protrusion might complicate delivery was already mentioned by Kuliga (1905) and later by Overgaard (1935). It is conceivable that a marked degree of acetabular protrusion might offer an insuperable obstruction to delivery, and although rare it should nevertheless be remembered as a cause of dystocia. It is noteworthy that in both cases recorded from our unit the presenting parts engaged only late in labour, in the first instance only 35 minutes before the baby was born, and in the second case only after labour had been in progress for 31 hours.

The absence of any pain or defective hip joint movements in Case 2 is also significant from a diagnostic point of view. This has also been recorded previously (Brailsford, 1953; Thoroughman, 1945). Case 1 was associated with an android pelvis. This association is stressed by Snow (1952) and is also mentioned by Greenhill (1955).

Brailsford (1953) has shown conclusively that this disease may be found at all ages, even in infancy. With the acceptance of this fact, the knowledge of the condition and the widespread use of radiography in obstetrics and otherwise, it is not improbable that more cases presenting with this abnormality of the bony architecture of the pelvis may be recorded in the future.

Summary

(1) The literature with regard to Otto's pelvis, i.e., intrapelvic protrusion of the acetabula, is reviewed.

(2) Two further cases are described, outlining some of the difficulties that may be encountered in patients suffering from this condition.

(3) The importance of the previous obstetrical history is stressed.

(4) With the increased use of radiography in obstetrics, together with the knowledge that this condition may be found in the younger age groups, an increase in the number of patients harbouring Otto's pelvis is predicted.

I wish to express my appreciation to Professor James T. Louw for his encouragement and helpful criticism.

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FIG. 1

(Case 1.) Inlet view of pelvis showing bilateral acetabular protrusion into the pelvic cavity (Otto pelvis), the android configuration of the inlet with the foetal skull overlying it.

FIG. 2

(Case 1.) Antero-posterior view of pelvis showing bilateral acetabular protrusion. The foetal skull overlies the pelvic inlet.

FIG. 3

(Case 2.) Inlet view of pelvis showing bilateral acetabular protrusion into the pelvic cavity (Otto pelvis).

FIG. 4

(Case 2.) Antero-posterior view of pelvis showing acetabular protrusion of milder degree than Figs. 1 and 2.

W.H.M.

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PREGNANCY FOLLOWING URETERO-COLIC ANASTOMOSIS

BY

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THE association of pregnancy with ureteric transplantation into the bowel, although still relatively rare, has become more common in recent years, as the operation is now more frequently undertaken in cases of irreparable vesicovaginal fistulae and in cases of congenital abnormalities of the urogenital tract, particularly in the condition of congenital exstrophy of the bladder.

A review of the literature has brought to light a total of 23 cases in whom pregnancy has occurred subsequent to the transplantation of both ureters into the sigmoid. In 20 instances the anastomosis was carried out because of the presence of exstrophy of the bladder, either as the initial treatment of the condition or following one or more attempts at plastic repair. In the remaining 3 cases transplantation was carried out after repeated and unsuccessful attempts to repair vesicovaginal fistulae.

One of the earliest cases of successful pregnancy following anastomosis was recorded by Mayo in 1919. This terminated in spontaneous delivery of twins. Grey Turner, in his personal series of cases of uretero-intestinal anastomosis, reported in 1929, describes one of his earliest cases treated in 1914, in whom pregnancy occurred 5 years after operation. This patient had 2 further uncomplicated pregnancies. Since these 2 occasions, 21 subsequent cases have been reported in the literature.

The following case which was recently dealt with in the Glasgow Royal Maternity and Women's Hospital, although similar to those previously reported, differs in that transplantation was carried out because of incontinence of urine resulting from injury to the urethra following fracture of the pelvis.

CASE REPORT

The patient, Mrs. A.H., in 1934, at the age of 3 years, sustained a fracture of the pelvis with laceration of the external genitalia and urethra. This was followed by incontinence of urine of gradual increasing severity eventually becoming complete both by day and night. At the age of 19 years in 1950, transplantation of both ureters into the colon was carried out. Rectal control thereafter although not complete was satisfactory. Post-operative urograms showed delayed excretion of the left kidney with dilatation of the left kidney pelvis and calyces and only slight dilatation on the right side.

The patient married in November, 1952 and in June, 1953 she became pregnant.

She was referred to the Antenatal Department of the Glasgow Royal Maternity and Women's Hospital in the sixth month of her pregnancy. She appeared in good health but complained of frequency of micturition with occasional incontinence of urine.

Examination of the pelvis revealed only a little scarring of the external genitalia but a wide separation of the symphysis pubis, the rami being united by a firm fibrous band. Over this area some tenderness was present. The sacral promontory was not reached, the sacrum was well curved and the pelvic outlet appeared to be wider than normal.

Immediately prior to admission for investigation the patient developed slight haematuria which lasted two days. She also had developed dysuria with increased frequency of micturition and pain in the region of the rectum.

She was admitted to hospital on 5th December, 1953. The uterus was enlarged to a size corresponding with a pregnancy of 30-weeks duration.

No tenderness was elicited on palpation of either renal region.

Intravenous urography showed delayed excretion and well marked dilatation of the left kidney pelvis and calyces, with only slight dilatation of the right kidney pelvis. Both ureters were dilated and showed slight kinking (Fig. 1).

It was considered, in view of the history of haematuria associated with the above findings, that the patient was suffering from a pyelonephritis affecting the left kidney.

The urologist who had carried out the transplantation was consulted. He was also of this opinion and agreed that unless the infection did not respond to treatment the

FIG. 1
Showing delayed excretion and hydronephrosis of left kidney.

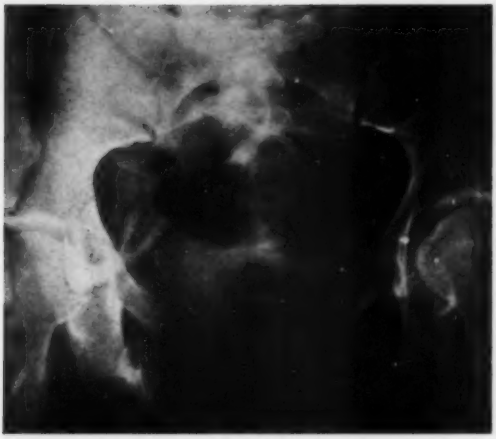

FIG. 2
Showing wide separation of symphysis pubis.

FIG. 3
Showing a minor degree of hydronephrosis of left kidney.

W.J.G.

pregnancy should be allowed to continue. Treatment with copious fluids, alkalis and sulphonamide was instituted. This was continued for six days until a total of 30 g. of sulphamezathine had been given. During this period there had been no recurrence of the haematuria, nor had there been any rise of pulse rate or temperature and the symptoms of frequency and dysuria improved.

Radiological pelvimetry was carried out and confirmed the clinical findings. The true conjugate diameter was found to be 4·3 inches, the transverse diameter at the brim 5·16 inches, lateral true conjugate diameter 4·34 inches, the oblique diameters each 4·39 inches, the posterior saggital diameter 1·64 inches and the inter-ischial diameter 5 inches. The wide separation of the symphysis pubis was obvious (Fig. 2) and the deformity of the lower part of the sacrum suggested a site of previous fracture.

The blood pressure throughout the pregnancy had not risen above 130/80 mm. of Hg. This state of affairs was maintained until the end of the pregnancy.

On biochemical analysis of the blood, the blood urea was found to be 33·5 mg. per cent, the total serum proteins were 5·37 g. per cent, the serum albumen 3·11 g. per cent and the serum globulin 2·26 g. per cent. The blood uric acid level was found to be 5·5 mg. per cent.

The patient remained well for the rest of her pregnancy although she complained of pain over the pubic symphysis and urinary incontinence increased until towards the end of gestation when incontinence became complete.

She was readmitted to hospital ten days before the calculated expected date of delivery although the height of the fundus suggested only a maturity of 36 weeks. Engagement of the head occurred three days after admission to hospital and was followed four days later on the 27th February by the commencement of labour. Pain over the symphysis was now a constant feature but was not severe. Labour progressed satisfactorily and after 12¼ hours spontaneous delivery occurred of a live mature female child weighing 5¾ pounds. It had been decided to carry out episiotomy but delivery of the foetal head was so rapidly and easily completed that episiotomy was considered unnecessary. The perineum and anal sphincter remained intact. The third stage of labour was normal, the placenta being expelled spontaneously five minutes after the birth of the child.

The patient stated that urinary continence returned on the first day after delivery; indeed she believed that she had more control than even before the pregnancy had occurred.

The puerperium was uneventful and the child progressed satisfactorily.

Biochemical analysis of the blood on the tenth day of the puerperium gave the following percentage results:

Blood urea	40 mg.
Total serum protein ..	6·8 g.
Serum albumen	4·4 g.
Serum globulin	2·4 g.
Blood uric acid	5·35 mg.

Intravenous urography carried out on the same day showed that the degree of hydronephrosis of the left kidney was less marked although excretion was still delayed. The right kidney appeared to function well. The patient was dismissed home well with the child, who was progressing satisfactorily, on the 9th March.

Follow-up. The patient reported back to hospital on 30th April, 1954. She felt well and had complete urinary control for 3–4 hour periods. The child continued to thrive.

Second pregnancy. On 17th December, 1954, the patient reported to the Antenatal Department of the Glasgow Royal Maternity and Women's Hospital in the 24th week of her second pregnancy. Once again her sole complaint was of gradually increasing incontinence of urine which had commenced during the second month of her pregnancy. The pregnancy progressed and the patient continued to remain well throughout the remainder of the pregnancy, the blood pressure remaining within normal limits.

Intravenous urography was carried out on 23rd December, 1954, and on this occasion a much lesser degree of hydronephrosis was present on the left side, the right side being normal (Fig. 3).

On 19th March, two days before her calculated date of delivery, the patient was admitted to hospital. The foetus was presenting as a vertex and the height of the fundus uteri suggested a maturity of 36 weeks.

On 22nd March, 1955, labour commenced spontaneously and after six hours spontaneous delivery of a live premature female child weighing 5¼ pounds occurred.

The puerperium was uncomplicated and again urinary continence returned completely immediately after delivery. The child progressed satisfactorily and both mother and child were dismissed home on 29th March, 1955.

Follow-up. The patient reported back to hospital on 21st April and made no complaints. Urinary continence was normal. The child continued to thrive.

Discussion

In a condition so infrequent in its occurrence as pregnancy following ureteric transplantation, it is not possible to state with certainty the effects of pregnancy on the mother and child.

In considering the advisability of allowing pregnancy to continue three factors must be borne in mind.

Firstly and most important, there is the effect of the pregnancy on the renal tract of the mother.

Since the transplanted ureter is usually inserted into the bowel at or below the level of the pelvic brim, the physical changes in the upper urinary tract produced by pregnancy are likely to be the same in the transplanted ureter as in the normal. The main difference between the two lies in the fact that the transplanted

ureter ends in an infected cavity whereas the bladder is normally free from infection. It would therefore seem imperative that, in order to avoid urinary infection, obstruction and stasis of urine flow, as frequently occurs in pregnancy, must be avoided at all costs.

From a review of the literature, this would not appear so difficult to achieve as might be imagined. In only 2 cases reported did infection of the renal tract occur during pregnancy. In one case (Randall and Hardwick, 1934) this was transient and responded rapidly to treatment. In the second (Hermann and Greene, 1944) the pregnancy was terminated in the sixth month because of "pyelonephritis". This patient, however, had a further pregnancy uncomplicated by renal infection. In the author's case a transitory haematuria with dysuria occurred in the sixth month of the first pregnancy but responded rapidly to alkaline and chemo-therapy. No such complication occurred in the second pregnancy. It would therefore seem justifiable to allow pregnancy to continue provided that renal function has been normal at the commencement of the pregnancy and that no gross renal infection is present. This is in agreement with the views expressed by Hinman (1951) and Lotimer (1954).

The other two factors, although not pertaining to the author's case, were of importance in the majority of the previously reported cases in whom transplantation had been carried out for the congenital abnormality of bladder exstrophy.

These are the subsequent development of genital prolapse and the possibility of transference of the congenital abnormality to the foetus.

The question of genital prolapse and its prevention in cases of this type has been discussed at length by previous writers. There seems little doubt that such a condition frequently follows vaginal delivery in such cases and would appear to be due to the association of a difficult labour with a congenital deficiency of the pubocervical fascia.

Bladder exstrophy is always accompanied by split pelvis in which, according to Williams, "owing to the descent of the promontory of the sacrum and the absence of union at the symphysis, there is marked transverse widening of the posterior portion of the pelvis while the anterior portions extend more or less parallel". It is his view that for practical purposes the pelvis may be considered as generally enlarged and that dystocia, which in his opinion is not common, is due to abnormalities of mechanism resulting from the absence of a resistant anterior pelvic wall. A similar view was held by Jellett (1910), but Miller and King (1918), in a review of the literature, found that of 14 cases only 4 had fairly easy deliveries.

Despite the conflicting views there can be little doubt that the advancing foetal head will take adavntage of the deficiency of the anterior pelvic wall and thus cause excessive bulging and overstretching of the congenitally deficient or even absent pubocervical fascia. This view is shared by Dawson (1933) and is supported by the statement made in the report of a case by Miller and King in which they say that "interference (in the form of forceps delivery) was necessary because the force of the labour pains was expended in producing a bulging downwards of the soft parts, with no real progress of the child".

In the case described, although there was separation of the symphysis pubis, this was not of congenital origin and was therefore not likely to be associated with a gross deficiency of pubocervical fascia. Dystocia therefore was not anticipated and events have since justified the view.

The third factor in considering the desirability for continuation of pregnancy, that of the transmission of the congenital defect to the offspring, although again not operative in the case described, deserves consideration. As already mentioned, in 20 of the previous cases reported, the congenital defect of bladder exstrophy was present, but in one of these alone (Pierce, 1931), one child (4 per cent) a male, of a total of 24 children born, exhibited a mild degree of hypospadias, the prepuce being split down to the frenum.

It would seem that transmission of the congenital defect is a rare occurrence and should not be considered as a contra-indication to pregnancy in such cases.

Antenatal Health. On reviewing the antenatal health of the cases reported, apart from the two

cases of pyelonephritis already mentioned and the single bout of pyelonephritis occurring in the first pregnancy of the author's case, little or no upset was noted in the antenatal period. Blood pressure and weight gain were normal. Renal function, as measured by estimation of blood urea, serum proteins and blood uric acid, appeared to be maintained throughout the pregnancy although excretion urograms carried out during the first pregnancy showed a slight impairment of function of the left kidney. During the second pregnancy, however, this was less apparent.

Urinary incontinence was never complained of in the cases previously reported and it is of interest to note that in the case described the patient did become gradually more incontinent during both pregnancies as the pregnancies progressed. This could have been attributed to pressure of the foetus on the bowel and to loss of tone of the sphincter muscles similar to that said to affect the bowel musculature during pregnancy. In view of the rapid return of continence after delivery it is more probable, however, that the incontinence was due to pressure alone.

Mode of Delivery. In regard to the mode of delivery, where bladder exstrophy, with the accompanying pelvic deformities and its attendant tendency to vaginal prolapse, is present, delivery by Caesarean section is a method favoured by many writers.

In the present review, in 18 cases the mode of delivery is known. Caesarean section was carried out in 7 cases in one of which (Green-Armytage, 1926) the indication for section was primarily the presence of a pelvic mass believed to be an old-standing inflammatory lesion. In two of those cases reported repeat Caesarean section was performed.

Vaginal delivery occurred in 11 cases (14 deliveries) and was followed by the development of vaginal prolapse in 4 instances (36 per cent).

Although this incidence is greater than the normal incidence of prolapse in women after childbirth it is not so great as might be expected in the presence of deficient uterine supports. It would not appear such a strong indication for Caesarean section as suggested by some writers.

This view is further supported by the report of the occurrence of prolapse in at least 3 nulliparous women suffering from congenital exstrophy of the bladder.

Where transplantation was carried out because of vesicovaginal fistulae Caesarean section must necessarily be the method of delivery since further damage to the birth canal would only result from vaginal delivery.

In the absence of bladder exstrophy and vesicovaginal fistulae, as in the present case, such considerations are less important. Although not entirely absent the dangers of vaginal delivery would be much less. The extent of fibrosis of the birth canal resulting from injury of the soft tissues, if great, might favour the employment of Caesarean section. In the case described scarring of the vulva and vagina was minimal, being confined to the region around the urethra. It was therefore decided that, in the event of labour progressing satisfactorily, vaginal delivery should be allowed and that an episiotomy should be carried out if necessary, before the perineum had become overstretched, since the all important factor in vaginal delivery in transplant cases is the preservation of sphincter control.

In order to preserve the anal sphincters from possible damage, episiotomy should be regarded as a necessary routine procedure in all cases in whom laceration of the perineum is imminent.

Late Results. Although in many of the cases reported the follow-up has been of short duration, nevertheless several cases have been reported as being alive and well as much as 10 years after the pregnancy and indeed several of the cases, including the case reported, have had successive pregnancies without any apparent renal impairment. One of Grey Turner's earliest cases was reported by him (1943) to be alive and well 29 years after the original operation, having had 3 successive pregnancies after operation.

It would appear that pregnancy does not cause any permanent impairment of renal function provided that renal function is satisfactory at the commencement of the pregnancy.

Conclusions

(1) The increasing employment of early transplantation of ureters into the colon will result in an increase in the number of patients in whom pregnancy occurs after this operation.

(2) Renal function would appear to be unimpaired by pregnancy and delivery.

(3) The incidence of genital prolapse in cases of congenital exstrophy of the bladder is greater both before and after pregnancy.

(4) Caesarean section is not necessarily indicated unless in cases of vesicovaginal fistulae.

(5) In cases of congenital exstrophy of the bladder transmission of congenital defects to the foetus is a rare occurrence.

(6) Early episiotomy is desirable although not always necessary in order to protect the anal sphincter.

(7) Provided that renal function is normal at the commencement of the pregnancy, the late results would appear to be unaltered by the occurrence of pregnancy.

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A CASE OF UTERUS PSEUDODIDELPHYS AND TWIN PREGNANCY

BY

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UTERUS didelphys, or uterus duplex bicornis cum septo vaginale, means complete duplication of the corpus uteri, cervix and vagina. This duplication very rarely extends to the vulva. Uterus pseudodidelphys means a double corpus and cervix, a vaginal septum having once been present, but since destroyed.

Duplication of the uterine body and cervix is rare. In 50,000 obstetrical cases in London and Liverpool, it was only noted on 5 occasions. Multiple pregnancies are uncommon, and none of these 5 patients had twins. It is proposed to present a case of a multiple pregnancy in a patient with uterus pseudodidelphys. This particular anomaly was previously classified as uterus didelphys, only the vaginal septum had been destroyed during her first confinement.

CASE HISTORY

Mrs. J.C.T., married, aged 30, first attended the Antenatal Clinic when 8 weeks pregnant.

Past Obstetric History. 1949: Eight-weeks abortion. At curettage a uterus didelphys was found, the pregnancy having occupied the right cavity. A hysterosalpingogram some weeks later confirmed the diagnosis (Fig. 1). The intravenous pyelogram was normal.

1951: Normal delivery of a full-time healthy infant. The vaginal septum was destroyed during the delivery.

This Pregnancy. The last menstrual period commenced on 24th October, 1952. She was admitted to hospital on 20th May, 1953, at 31 weeks, for antenatal rest. At this time her uterus was enlarged to the size of a pregnancy of 34 weeks. Twins were diagnosed and confirmed radiologically (Fig. 2).

Labour. She was readmitted to hospital in strong labour on 6th July 1953. Each foetus presented by the vertex. After 2 hours the first child was born normally from the left uterine cavity. Immediate vaginal examination showed the right cervix to be fully dilated, and the second twin was delivered 5 minutes later. After 0·5 mg. of ergometrine had been given intravenously, the left placenta was expressed easily. The right was retained and necessitated a manual removal. The total blood loss was 10 ounces. The babies were of different sexes, both of blood group "B" rhesus positive, and weighed 5 pounds 6 ounces and 5 pounds 14 ounces respectively. The placentae were quite separate.

DISCUSSION

The presented case is unusual in that both sides of the uterus pseudodidelphys were in labour simultaneously. With complete uterine duplication and a pregnancy in each side, case reports show that there is usually a considerable interval between the birth of the two babies. It has varied from 15 hours to 59 days. This is of interest as it suggests that a local stimulus plays a major part in the onset of labour. The birth weights of the babies, if they reflect the stages of development, are compatible with the twin pregnancies starting at the same time, there being no clear evidence of superfoetation.

It is unfortunate that Polak's (1923) figures on the frequency of twin pregnancies are often quoted. He states that a single pregnancy is only 7 times commoner than a multiple in uterus didelphys. Eighty-eight reported cases of complete uterine duplication were associated with 7 multiple pregnancies and 136 single pregnancies. This represents an incidence of 1 in 16·5. As many single pregnancies in double uteri are not

reported, and often the anomaly is not recognized, it is thought that multiple pregnancy is not as common as these figures indicate.

Premature labour, post-partum haemorrhage and retained placenta are common complications. Post-partum haemorrhage and manual removal of the placenta occurred twice in the 7 reported cases.

Summary

(1) A case of uterus pseudodidelphys with a twin pregnancy is presented.

(2) The incidence and complications of multiple pregnancies in completely duplicated uteri are discussed.

Acknowledgments

I wish to thank Mr. E. D. Y. Grasby, of Pembury Hospital, Kent, for permission to publish this case, and also Mr. Victor Lack for his comments.

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FIG. 1
Hysterosalpingogram showing double Cervix and Corpus Uteri.

FIG. 2
X-ray showing two foetuses.

GENETIC SPECULATION BASED UPON ANIMAL EXPERIMENTATION IN RELATION TO ACTUAL HUMAN EXPERIENCES, IN THE TREATMENT OF FEMALE INFERTILITY AND STERILITY BY X-RAY THERAPY

BY

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THAT X-ray therapy for the relief of female infertility and sterility is an effective therapeutic procedure is borne out by the results obtained by me over the course of the past 30 years in the treatment of more than 700 women referred for irradiation. An appreciable number of these women are known to have conceived and borne more than 400 normal children. Of these latter, 26 children, that is, grandchildren of the originally treated women, have already been born. All these children are normal, mentally and physically, many having been followed up for more than 18 years.

Adverse criticism of the use of irradiation for the treatment of female sterility has been voiced by one, whose speculation as to probable genetic effects of such irradiation is based solely on animal experimentation, and his experiences are in direct contrast with the documented and readily observable results noted in a vast number of treated human beings.

In a recent issue of the *Journal* (Rugh, 1955), unfavourable comment interlaced with erroneous statements and with some unfair personal attacks on the author are made, which demand a reply. Rugh not only unwarrantedly rebukes the obstetrician and gynaecologist, but failed to note that I am neither, being distinctly a radiation specialist, of many years' training and experience, with considerable knowledge of radio-biology. These unfair statements were made by Rugh even though admittedly he personally has had no experience in the treatment of human beings with irradiation.

In this article a statement is naïvely made that my work, as reported by me (Kaplan, 1953) for the treatment of female infertility, lacks controls. Unlike those who work only in animal experimentation, my experiences are entirely clinical, based upon readily observable effects in human beings, the best of all controls. The geneticist has also failed to recognize that, before irradiation was administered, these infertile women had received every other type of therapy without avail.

Whether or not irradiation to the pituitary alone will achieve favourable results is problematic. In my reports I have stated that in my hands irradiation only to the pituitary rarely relieved the sterility condition. For this reason, irradiation to the pituitary and the ovaries was administered simultaneously in all cases of infertility and sterility treated by me.

Lack of adequate knowledge, no doubt, permits the geneticist erroneously to state that there is no difference between whole body irradiation and that administered to a specific, limited area. That there is a significant difference has been definitely established by the physicist, as well as by the radiologist. Deringer, Lorenz and Uphoff (1955), recently reporting on the effect of irradiation on mice, state: "The greatest effect of X-radiation was noted when animals received irradiation to the whole body, a lesser effect when ovaries alone were irradiated, and least effect when whole body irradiation with the ovaries shielded."

It should be of keen interest to know how the geneticist explains the favourable result in the case of a young married woman who, following

X-ray castration, later resumes menstruation after an amenorrhoea of 3 years, conceives and bears 2 normal children. Such a sequence of events was recently reported by me (Kaplan, 1955). In this case, a young married woman (age 27), was sterilized by X-ray therapy in 1946 and remained amenorrhoeic for 3 years. Menstruation was then resumed spontaneously; she readily conceived and bore 2 normal children, a girl on 31st March, 1951, and a boy on 23rd September, 1954.

In 1905, Halberstaedter noted that X-rays had a selective action on the ovaries. How then does the geneticist explain the resumption of normal menstruation, apparent regeneration and development of normal ova, capable of fertilization and developing into normal progeny, after X-ray castration? Ellinger (1956) says: "it appears that the irradiation dose must have been borderline, between the dose that just suppresses menstruation, and that which irreversibly destroys ovulation. While the recovery of the ovary to a usually adequate 'castration dose' is explainable in the light of the aforementioned facts, the explanation of the mechanism of such recovery remains unknown."

Whether irradiation increases the probability of genetic damage to the offspring of women who later conceive following X-ray castration, is still not definitely proved. According to Muller (1954), "the damaging of future generations caused by the application of radiation in the gonads is not a controversial question. The only question is how much damage is caused by a given dose." However, up to the present time, no one has been able to demonstrate the occurrence of genetic abnormalities; which are comparable to those noted in experimental animals, in the progeny of women irradiated by the small dose of X-ray used in the treatment of infertility. The birth of normal children to women, who previously had prolonged irradiation amenorrhoea, gainsays Muller's (1950) statement, that genetic damage is most likely to appear in the first generation following irradiation. Therefore, since the large dose of irradiation, used for castration, does not adversely affect the progeny of the irradiated mother, it is quite evident that the very small dose of X-ray used in the treatment of female infertility would scarcely have a harmful effect on the children of the irradiated mother.

This conclusion is further supported by the report of Neel and his co-workers (1953), who investigated the effects of irradiation from the atomic bombs on the progeny of exposed Japanese women who obviously received an amount of irradiation immeasurably greater than that employed for the therapeutic treatment of infertile women. They state: "There is no indication from this study of any unusual sensitivity of human genes to irradiation." More recently, Holmes and his associates (1955) stated: "no genetic effects have been observed in the first generation of children born to persons exposed at Hiroshima and Nagasaki." These findings are in accord with the observations made by me over the past thirty years, following the irradiation of more than 700 married women for infertility and sterility.

In his criticism Rugh (1955) goes out of his way to condemn the obstetrician who nowadays quite properly advises therapeutic irradiation for the infertile female who ardently desires a child, and who has already submitted to all other types of treatment without avail. The obstetrician now has definite proof of the effectiveness and harmlessness of irradiation, for no one—not even the geneticist—has demonstrated the birth of an abnormal child following proper irradiation for infertility. On the contrary, based on experience of over thirty years, I have reported the birth of upwards of 400 children and 26 grandchildren, born to irradiated women. None of these children—in the opinion of the paediatricians who have examined and followed some of them for 18 or more years—have exhibited any recognizable genetic injury. The fact too, that children of irradiated mothers have themselves produced normal children, is proof of the harmlessness of therapeutic irradiation for female sterility. Furthermore, the report of McIntosh and his associates (1954) on the occurrence of abnormalities in children born to women who have had no irradiation, is in striking contrast to the absence of abnormal children in my series. These workers report that 7 per cent of all pregnancies observed over a 5-year period at the Babies Hospital and the Sloane Hospital

for Women, in New York City, resulted in the birth of abnormal children.

Based on these facts, despite the non-clinical opinion of the geneticist to the contrary, history may well record the normalcy of future generations born of women irradiated for sterility and treated by "such as Kaplan". Because of age limitations, I fear I shall not be vouchsafed the pleasure of seeing the happiness of the many women I treated during many years, who have achieved motherhood and grandmotherhood because of X-ray therapy. I believe that Rugh and those who think like him are—to be charitable—just as likely to err on their side, as they predict does the "genetically untrained obstetrician". No one can blame the geneticist for having prevented some women from experiencing motherhood, except that he claims this inhibition solely on the ground of animal experimentation, without cogent proof so far adduced in the human species, showing parallel mutation effects. In the paper by Rugh, he has seen fit to condemn irradiation of the ovaries as if they were testes. He goes out of line to describe the effects of irradiation on the male gonads, ignoring the fact that in my report, to which he has taken exception, no mention is made of irradiation of the male. His discussion of the male reaction to irradiation is, therefore, entirely irrelevant to this discussion.

My report, based on clinical human and not animal experimentation, bears out the assertion by Rubin (1952), Israel (1952) and many others, that irradiation, when properly administered for the treatment of female infertility and sterility, has not produced abnormal genetic effects on the second or third generation offspring of irradiated human females.

Conclusions

The relationship of authentic clinical results of irradiation of infertile human females in contrast to genetic speculation based solely on animal experimentation is discussed. Contrary to the statements of the geneticist, no one has demonstrated the birth of an abnormal child following properly administered irradiation of the mother for infertility and sterility. On the contrary, published records reveal that an appreciable number of abnormal children have been born to women who never were irradiated.

Despite the predictions of the geneticist, no detectable genetic abnormalities have been noted in the first generation children born to a large number of therapeutically irradiated women.

Because no abnormalities have been observed in the grandchildren of treated women over the course of 10 or more years, prediction of further genetic abnormalities in the progeny of irradiated women is an unwarranted speculation, based solely on animal experimentation and not substantiated by clinical human results.

Based upon the clinical observation of more than 700 married women treated by me with X-ray therapy, I believe I may properly reiterate that the results of irradiation for infertility and sterility in human females, are harmless to the treated women, their children and their children's children.

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FERTILITY AFTER TUBAL PREGNANCY*

BY

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IN the practice of medicine one important function of the doctor is to give a reasonably reliable prognosis, both immediate and remote. A few years ago we investigated the prognosis in the case of women complaining of primary infertility, and our results suggested that about 50 per cent became pregnant sooner or later, although in not more than half could the success be attributed directly to medical treatment (Bender, 1952). More recently an enquiry has been made into the prognosis for childbearing in women who have had a tubal pregnancy. This is a subject on which little has been written; the most recent major contribution was made by Grant in Australia in 1953.

MATERIAL

The material for this investigation comprised 305 women who were operated on for tubal pregnancy during the years 1946–1952 inclusive, in nine hospitals in the Liverpool area: Broadgreen Hospital, Chester City Hospital, Liverpool Royal Infirmary, Mill Road Maternity Hospital, Sefton General Hospital, Stanley Hospital, Walton Hospital, Whiston Hospital and The Women's Hospital. I am grateful to the consultant gynaecologists of these units for allowing me access to the case-records and for permitting me to follow up these women. A follow-up was obtained in 264 of the 305 patients, a percentage of 86·5. In addition, several others were traced but were found to have left the country. The figures given hereafter are in relation to the 264 cases followed up and not to the total 305.

* Presented to the Combined Annual Meeting of the British and Canadian Medical Associations, Toronto, June, 1955.

CONCEPTION RATE

Of the 264 women, 116 (44 per cent) became pregnant one or more times after their operation. It is easier to demonstrate the outcome in terms of percentage (Table I).

Of each 100 women who have had tubal gestations, on the basis of this follow-up 56 do not conceive again and 44 do. Of the 56 who remain sterile, 7 have had a sterilizing operation, either both tubes having been removed (separately or at the same operation) or hysterectomy having been performed. In another 6, the remaining tube has been shown by salpingography to be blocked. There must be others in whom the remaining tube is blocked but it has not been proved. In addition, at least 3 of the 56 do not become pregnant because they consistently practise contraception. There are more than 3 who avoid pregnancy, but these 3 volunteer that they contracept purely for fear of another ectopic pregnancy.

TABLE I

Conception Rate Following Tubal Pregnancy

100	56 do not conceive again	7 have had sterilizing operation.
		6 other tube proved blocked.
		3 contracept.
	44 conceive again	32 have living child.
		5 have abortion only.
		7 have another tubal pregnancy.

In 44 of the hundred, conception does occur again; but this is a minimum figure because of the limited time of follow-up, at the most 7 years. If all of these women were followed to

the menopause the conception rate would probably approach 50 per cent. Of the 44 who do conceive, 32 produce live babies. This means that only 1 in 3 women who have had a tubal pregnancy will thereafter have a live child. Five of the 44 have abortions only. Finally, 7 of the 44 have a further ectopic pregnancy, a high rate of 16 per cent.

It is interesting to compare the outcome in this group of women with that in cases of primary infertility (Table II).

TABLE II
Comparison of Outcome
(Percentages)

	Primary Sterility	After Tubal Pregnancy
Conception rate	46	44
Living baby	36	32
Abortion only	9	5
Ectopic pregnancy	1	7

The conception rate and the number who have living children are similar in both groups. Abortion may be a little more likely in the primary sterility cases, but in both the incidence of ectopic pregnancy is greatly increased. The incidence of tubal gestation in general is given as about 0·3 per cent. Our 1952 figures suggested that it is increased sixfold in women who conceive after having been seen on account of primary infertility, a finding since confirmed by Swyer (1953) in London and by Grant (1953) in Australia. The present figures suggest that, if a woman conceives after a tubal pregnancy, her chances of a further ectopic gestation are increased almost fifty-fold.

It should be borne in mind that these two groups present one basic difference. Those women with primary sterility sought medical aid on that account, whereas the other group were sought out by the doctor and only a few of them complained specifically of infertility. This is largely because 75 per cent had already had at least one living child.

FACTORS AFFECTING THE CONCEPTION RATE

Age. The conception rate was notably higher in the 130 women under the age of 30 at the time of operation (54 per cent) than in the 134 older patients (34 per cent).

Parity. The conception rate was the same in the previously parous and the previously nulliparous.

Type of Operation. Of particular interest is the relationship between the type of operation performed and the subsequent conception rate (Table III).

TABLE III
Conception Rate Related to Type of Operation

Operation	No.	Conceived	
Laparotomy only	4	4	
Salpingotomy ..	4	3	(1 tubal)
Salpingectomy	187	80	(13 tubal)=42·7 per cent
Salpingo-oöphorectomy	51	29	(4 tubal)=56·8 per cent
Sterilizing ..	18	0	
Total ..	264	116	(18 tubal)

In 4 women at laparotomy nothing was done because tubal abortion was seen to be complete; all 4 became pregnant again. This is a reminder that probably most cases of tubal pregnancy are never diagnosed. Probably the commonest fate of the fertilized egg which implants in the tube is that it dies and is absorbed. The patient is unaware that conception has occurred and medical aid is not sought. There must also be a proportion of cases of complete tubal abortion in which the symptoms are so minor or of such short duration that the doctor is not called.

Of the 4 women on whom *salpingotomy* was performed, 3 became pregnant again, 1 of them in the same tube. The fourth patient had a salpingogram which showed that neither tube was open. Further reference will be made to the place for salpingotomy.

In the majority of cases (187) *salpingectomy* was carried out and 80 of these women became pregnant again, a conception rate of 42·7 per cent. In 51 women *salpingo-oöphorectomy* was performed and 29 of these became pregnant again, a conception rate of 56·8 per cent. Statistically the difference between these rates is barely significant, but from a practical point of view two further factors must be considered in this relation. The first is the argument put forward by Jeffcoate (1955), based on the fact

that ovulation is primarily controlled by the anterior pituitary gland. If one tube is removed, the ova produced by the homolateral ovary, which will be about half of all ovulations, are likely to be lost for fertilization. But if the homolateral ovary is removed with the tube, ovulation is thereafter confined to the one remaining ovary, which has a tube adjacent, and all ova will have a reasonable chance of fertilization. Secondly, perusal of the records reveals that salpingo-oöphorectomy was more often carried out either when the patient was older, or when the surgeon was comparatively inexperienced, or when the condition of the patient was so grave that the quicker operation of removal of the whole appendage was performed, points which might unduly weigh adversely against further pregnancy in this group. It is suggested, therefore, that pregnancy is more likely to occur again when tubal pregnancy is treated by removing tube and ovary rather than tube alone.

The Non-pregnant Tube (Table IV)

The condition of the non-pregnant tube was not always detailed in the operation records, but it was noted at operation in 18 that this tube was, or had previously been, removed.

In 26 cases the opposite tube was adjudged closed. Judgment on this point at the time of operation is not infallible, and indeed in 2 of these 26 women a further pregnancy, intrauterine in both cases, occurred later. In 9 of these 26 women *salpingostomy* was performed at the time of laparotomy for the tubal gestation. In 2 of the 9 a further pregnancy occurred but it was tubal in both cases. In 1 of these 2 patients the salpingostomy had been commenced but abandoned as hopeless! In one other of the 9, the excised portion of tube showed the presence of tuberculosis. In another 3, salpingograms later showed that the end-result was a hydrosalpinx; and in the remaining 3 the patency of the tube is not known. In another 12 women the non-pregnant tube was noted to be damaged although not definitely closed; none conceived again.

In 14 women tubal patency was tested some time after operation. In 8 the remaining tube was found to be open and 4 became pregnant, one having a further tubal gestation. The other 6 showed no tubal patency and did not become pregnant.

The Management of Tubal Pregnancy

The results of this enquiry may therefore offer some guidance in the management of tubal gestation in women who wish to become pregnant again.

Firstly, the non-pregnant tube should be inspected and its condition detailed in the operation records. In one hospital one gynaecologist always tested the patency of the non-pregnant tube by retrograde insufflation and apparently without ill-effect in any case. In theory at least, this practice involves a small risk of air embolism.

It would be preferable to inspect the non-pregnant tube before dealing with the affected side. For example, in one woman it was fortunately noticed that the opposite tube was rudimentary. Salpingotomy was therefore substituted for the projected salpingectomy, and this patient was delivered of a living baby last year. It is suggested that there is a much larger place for salpingotomy than is generally conceded.

Table IV
State of the Non-pregnant Tube

Noted at operation	Removed 18	
	Found closed 26—Salpingostomy in 9	3 hydrosalpinx 1 tuberculous 3 unknown 2 conceived (both tubal)
	Found damaged 12	
Tested after operation	Found open 8—4 conceived (1 tubal)	
	Found closed 6	

In particular, it gives better results than carrying out salpingostomy on the other tube when blocked.

If salpingotomy is not feasible and the woman wishes to become pregnant again, a better prognosis follows if the ovary is removed together with the offending tube.

At operation as much clot and blood as possible should be removed in order to minimize subsequent adhesions or infection. Grant (1953) described a number of women with infertility in whom salpingography showed that both tubes were open. These women then had tubal pregnancies and in more than half of them the remaining tube was found, some time after operation, to be closed. He therefore advises post-operative chemotherapy as a routine.

Finally, the patency of the remaining tube or tubes should be tested as early as an intervening menstruation and the absence of infection will allow (Cook and Butt, 1953). Ovulation is usually resumed in the first cycle after the end of an ectopic gestation (Siegler, 1953). And if it is believed that fertility remains high after the end of a pregnancy, successful or unsuccessful, then it would be best to apply any therapeutic effect salpingography may have, as soon as possible.

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CONGENITAL ATRESIA VAGINAE

A New Modification of the Brady-Graves Operation

BY

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CONGENITAL absence of vagina is a rare abnormality. It may be complete or incomplete. Partial atresia of the vagina is not usually associated with any other gross deformity whereas complete atresia of the vagina is associated with the absence of the uterus. This is supported by McIndoe's series (Berkeley and Bonney, 1947) of 46 cases in which only one case had a functioning uterus. The problem is serious in these cases due to the absence of the uterus because, even after making an artificial vagina, the functions of menstruation or childbearing cannot be restored.

Various operations have been devised for the formation of an artificial vagina. Such operations as those of Baldwin and Schubert are serious, as a loop of intestine is used in these operations, which in some cases involves a risk to life. Graves's operation and its modifications, where an artificial canal is formed from flaps of labia minora and surrounding skin, is quite successful but the parts are grossly mutilated. McIndoe's operation, in which skin graft is used on mould, gives very good results. But in this operation skin graft is taken from the thigh which is a somewhat painful condition to the patient and special skill is required in cutting off the large one-piece graft (Berkeley and Bonney, 1947). There are simple operations, also, like Frank's and Wharton's but the results are not uniform and failures are noted. A great deal of patience is required both on the part of the patient and the doctor. The mould has to be worn for 3 to 4 months, which is inconvenient.

Having been dissatisfied with the results of these operative methods the idea struck me that, if one could implant a good flap of skin or mucous membrane with the blood supply intact to one wall of the artificially made vagina throughout its length, it should be successful in maintaining the patency of the canal. The idea of constructing this flap was taken from Brady's modification of Graves's operation for the formation of a vagina.

I am convinced, from the experience of 6 cases, that this new modified operation is a safe, very simple and theoretically sound method to follow. Any gynaecologist experienced in perineal operations can do it safely and with confidence of a good result.

The following is the report of the first case treated by this modified plastic operation.

Case 1. A girl of 15 years, was admitted on 22nd January, 1953, to the Maharaja Tukojirao Hospital, Indore. She was married 3 years before. She complained of difficulty of marital relationship and absence of menstruation; otherwise she was normal.

On examination it was found that the external genitalia were normally developed, but there was complete atresia of vagina. Per rectum examination showed that the uterus was absent, but that both the ovaries were present.

The operation was done as follows:

(1) A transverse incision was made just under the urethra from one labium minus to the other. The two ends of the incision were extended downwards and laterally through the skin of the perineum. This flap of mucous membrane was dissected downwards (Figs. 1 and 2).

(2) At the level of the muco-cutaneous junction the fibrous tissue was cut through with a few nicks of the scissors and further separation was done by finger pressure and cutting between bladder and rectum until a canal of about 3 to 4 inches was made. Care was taken not to open the abdominal cavity (Fig. 3).

(3) The flap of mucous membrane can be stretched to a sufficient length by incising the connective tissue just underneath it. The lateral incisions in the skin may be extended downwards if required, in order to secure

FIG. 1

Shows the demarcation of the flap in the mucous membrane and skin.

FIG. 2

Shows the flap dissected and turned down.

sufficient length of the flap, i.e., from 3 to 4 inches, depending on the length of the canal made. The upper edge of the flap is stitched to the top of the artificially made vagina, and the sides were stitched up to the lateral walls by interrupted sutures (Fig. 4).

A wax mould covered with a double layer of condom was introduced into the canal but it could not be retained and fell out. This led me to devise a method by which the mould could be retained inside. The vaginal opening was temporarily closed by passing three strong linen stitches through the labia majora to bring them together—thus the mould was kept in place (Fig. 6). A self-retaining catheter was put in, and a T-bandage was applied.

She was given a constipating mixture, with a low residue diet and antibiotics. There was swelling of vulva on the seventh day of the operation and the stitches in the labia majora were removed. When the stitches were removed, the mould was expelled spontaneously.

The posterior wall of the vagina was completely covered with the mucocutaneous flap. The patency of the canal was maintained. The three raw walls of the canal were covered with bleeding granulation tissue. The wound healed completely on the fourteenth day except for a small area about 2×2 mm. just anterior to

FIG. 3

Shows the hole made in the space between bladder and rectum.

FIG. 4

Shows the flap stitched up to the posterior wall of the tunnel by interrupted sutures.

FIG. 5
Shows the wax mould put inside the tunnel, i.e., the artificial vagina.

FIG. 6
Shows the three silk sutures passed through the labia majora to hold the mould in place.

FIG. 7
The mould.

the edge of the mucous membrane at the top, which healed later on without much difficulty.

Examination on the fourteenth day revealed that the vagina measured about 3 inches in length and admitted two fingers easily.

Six cases have been operated on by this method so far and the results are very good.

I followed up the cases and found that the artificially made vagina had increased in all dimensions and there was no complication.

The following is the short history of 5 other cases operated on by the same method.

Case 2 was operated on on 1st January, 1953. She was 20 years old and was married 5 years ago. She complained of primary amenorrhoea and stress incontinence for the last 8 months. She had no difficulty in coitus. On examination it was found that her urethra was markedly dilated and admitted two fingers easily and the contraction of the internal sphincter of the bladder could be felt on the examining fingers. There was complete atresia of the vagina. The uterus was absent.

Case 3 was operated on on 13th May, 1953. She was 21 years old and was married 4 years ago. She was average in development. She complained of difficulty and pain and dissatisfaction in coitus. She had complete atresia of vagina and the uterus was absent.

Case 4 was operated on on 9th August, 1953. She was 25 years old and was married 10 years ago. She was well developed. She complained of primary amenorrhoea, spotting after coitus occasionally, and sterility. There was no difficulty in coitus. On examination it was found that the urethra was dilated and admitted one finger easily. She had complete atresia of the vagina. The uterus was absent.

Case 5 was operated on on 22nd May, 1954. She was 28 years old and was married 10 years ago. She complained of primary amenorrhoea and sterility. The coitus was normal but occasionally painful and unsatisfactory. On examination it was found that the urethra was normal but just below the urethra there was a depression at the site of vagina. There was complete atresia of the vagina and the uterus was absent.

Case 6 was operated on on 16th March, 1955. She was 18 years old and married 6 months ago. She was brought for examination with the complaint of amenorrhoea. On examination of the case it was found that she had complete atresia of vagina. On P.R. examination, a small knoblike thickening of 1 cm. $\times$ 1 cm. was felt at the site where the cervix could be felt in a normal case. During operation, it was found to be a fascial sac only.

FIG. 8

Photograph of the case on the 15th day of the operation.

All the cases were followed up after a month with instructions to report immediately if any trouble arose.

All the cases were married girls and 3 of them reported that the operation was satisfactory. Out of these cases 2 had a markedly dilated urethra. On close enquiry and examination it was found that in one case the urethra was actually being used for coitus. In this case two fingers could be easily passed through urethra and at the top, at the level of the internal sphincter of the bladder after slight resistance, the sphincter gave way and the fingers could be introduced into the bladder. There was no cystitis. She complained of stress incontinence for the last 8 months. This case complained of an unsatisfactory result to the operation for 3 months because of the insufficient length of vagina. But subsequently on examination it was found that the vagina was more roomy. The patient said that for the past two or three months the urethra was not used for coitus and that she was satisfied with the operation.

It was observed in the other 3 cases, also, that the dimensions of the artificial vagina had increased on all sides; this is a definite advantage in this operation as the walls of the canal are capable of expanding.

Comments and Discussion

The operation method used in these 6 cases is very simple. There is no risk to the patient.

The mucocutaneous flap has a blood supply which is intact and so will hold.

The patency of the vaginal canal is maintained more easily because of the mucocutaneous flap.

The mould is kept inside the vagina for only 6 days. The method of retaining the mould inside is very simple and sound. The patient is allowed to walk about on the 10th day after the operation.

The healing takes place in fourteen days and all the granulation tissue disappears by the twenty-first day.

The appearance of the external genitalia is perfectly normal after the operation.

The vaginal canal made artificially enlarges in all dimensions later on because of coitus.

The mould can be easily made of wax. It should be of oval shape. Various sizes should be ready for use. It should be of small size, 1½–2 inches in length and 1¼ inch in diameter at the centre and tapering at ends. The idea of introducing the mould inside the artificial vagina is to keep the raw wall of vagina apart till the mucocutaneous flap holds; this takes only 6 days. The mould chosen should be of such a size that it can be easily introduced into the canal and there should be no undue tension on the walls. Two to three sutures are passed through the labia majora on both sides and tied together to hold the mould inside. This is a very important point in this method of operation as there is no undue pressure on the surrounding parts and so there is no danger of fistula formation as Wharton (1946) mentions. Even in McIndoe's operation this complication had occurred (Berkeley and Bonney, 1947). This method of keeping the mould inside is also important because if accidentally rectum or bladder is opened up there is no danger of fistula formation after repair as there is no undue tension.

The balsa wood mould which is used in Wharton's and other operations is probably too big in size because the idea is to keep the graft in contact with the canal and so damages the walls and fistula takes place by perforating through rectum. Such an accident is not possible in this method of operation as the size of the mould is so small that it is expelled spontaneously as soon as the sutures are removed. This method of keeping the mould in place is very simple, painless and there is no discomfort to the patient at all.

There is another kind of accident mentioned in some cases—the mould being very small, the perineal muscles closed over it, and subsequently it escaped through perforation in rectum. Such an accident is never possible in this new modified operation as the opposed surfaces of labia majora are not raw and as soon as stitches are removed, one is relieved and delighted to see the excellent result of the operation. The mould comes out spontaneously or on slight straining by the patient, the muco-cutaneous flap on the posterior wall is snugly fitting and looking healthy and live. The three remaining walls are covered by healthy granulation tissue.

The external genitalia are perfectly normal in appearance.

The after treatment is very simple and the mould is not worn any longer. The complete healing takes place in 10–15 days, after the removal of the mould. In Wharton's and all other operations, the mould is worn for one to four months with various ingenious methods which are inconvenient to the patient and too elaborate to execute.

The case and diagrams were shown in the Medical Association Meeting of Indore.

I am thankful to Mr. V. Apte and Mr. C. Wankar the Artists of our College who prepared the drawings.

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ANAEMIA IN PREGNANCY

As Encountered in Malaya

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IN Malaya anaemia is widespread and severe (Burgess, 1948, 1950; Read, 1951; Eagland, 1952; Lamprell and Cheek, 1952). For example, the mean haemoglobin level of Indian women rubber estate labourers is about 10 g. per cent (60 per cent Haldane). This state of affairs is sharply reflected in the high incidence of anaemia amongst pregnant women, always the most susceptible group of a population. It is thought that the experience of a large obstetrical unit, situated in the General Hospital, Kuala Lumpur, might be of comparative interest to workers elsewhere.

THE SOCIAL BACKGROUND

This hospital serves a population of about half a million people, although many normal deliveries are undertaken in homes or small district hospitals, and it caters principally for those of the lower income groups. The patients are mainly Southern Indian labourers working on rubber estates or employed on contract work for State and Municipal authorities; Chinese, who are usually artisans, small shop-keepers, labourers on tin mines, or building labourers; and a few Sikhs and Malays.

Nutritional surveys have been carried out on representative Indian and Malay populations (Burgess and Laidin, 1950) and show the strong tendency for these populations to exist below or only at the border line of adequate nutrition. There are no recent reports of surveys on other population groups available, but the general impression suggests that the same state of affairs exists, although as a whole Chinese have a better diet than other races.

ADMISSION TO THE UNIT

Patients attending the antenatal clinics of the hospital had their haemoglobin checked roughly at each visit, using the Tallqvist method. If the result was suspiciously low, it was repeated, using the Sahli acid haematin method. Those women with a haemoglobin of 6 g. per cent or less were admitted for treatment, while those with a haemoglobin between 6 and 8 g. per cent were treated and watched in a special anaemia out-patient clinic. The remaining patients attended the antenatal clinics and were given ferrous sulphate, 6 to 12 grains daily by mouth. If any fall in the haemoglobin level was detected at a subsequent visit, the patient was admitted and an attempt made to find the reason for this fall. About 80 per cent of patients delivered in the hospital attended the antenatal clinics.

During 1954, out of 5,550 admissions with 4,762 deliveries, 200 women were admitted in the antenatal period for the treatment of anaemia and a further 96 were treated in the puerperium —a total of 5·3 per cent of all admissions. In 1953 the incidence of admissions for anaemia was 6·3 per cent.

When admitted, the patients were investigated haematologically in more detail. Routine examinations undertaken were the haemoglobin level by the cyanhaematin method, red and white cell counts, and the packed cell volume. From these were calculated the mean corpuscular haemoglobin concentration (MCHC) and the mean corpuscular volume (MCV). Also, in the majority of patients examined in detail, a bone marrow smear from the iliac crest was examined.

Clinical Findings

It was found that symptoms only developed in these patients when the haemoglobin level had fallen to 6 g. per cent or less. The symptoms and signs were usually those common to any severe anaemia of slow onset, and they gave little indication of the cause of the anaemia. Occasionally, a patient with a severe megaloblastic anaemia showed clinical icterus, a sore and smooth tongue and diarrhoea, which in the absence of other causes suggests this type of anaemia.

Two clinical patterns which may lead to confusion in differential diagnosis have been encountered quite frequently. Severe anaemia appeared sometimes with signs suggestive of pre-eclampsia, namely a raised blood pressure, severe oedema and occasionally albuminuria (although the latter is always less than 0·5 g. per litre of urine by Esbach's method). These signs rapidly disappeared with rest in bed, although the oedema may linger if treatment of the anaemia is inadequate. Also severe swinging fevers were found with no apparent infective cause and were unresponsive to any antibiotics. This picture appeared most often in patients with severe megaloblastic anaemia and adequate treatment of the anaemia brought the fever down quickly. This state was particularly confusing in the puerperium.

Laboratory Findings

When dealing with nutritional anaemia, in which a megaloblastic element might be present, many workers have realized that examination of the bone marrow is imperative if a precise diagnosis is required (Trowell, 1951; Kothari and Bhende, 1952; Clark, 1952; Callender, 1944; Tasker, 1954).

The anaemias encountered among our patients in 1954 have been divided into a number of types, as shown in Table I. This classification depends mainly on the marrow picture, which, however, could not always be undertaken. Groups I–III are self-explanatory. Those in Group IV were admitted with a normoblastic marrow but, on treatment with iron, developed into a severely megaloblastic picture. Those in Group V are presumed to have been iron deficient, because they responded well to iron, but detailed haematological studies were not made. Group VI were patients with haemolytic anaemia associated with infections. Group VII were patients treated at once, without further investigation, and who responded well to iron and folic acid, and hence the type of anaemia is unknown.

Table I

Showing the Incidence of the Types of Anaemia as Encountered During 1954
Total Admissions 5,550

Group	Haemoglobin g. per cent			Total No.
	0–2·49	2·5–4·99	5–6·5	
I—normoblastic ..	3	52	25	80
II—intermediate megaloblastic	1	13	10	24
III megaloblastic ..	1	30	20	51
IV—normoblastic to megaloblastic	1	3	3	7
V—marrow unknown presumed iron deficiency ..	0	18	73	91
VI—haemolytic ..	0	1	2	3
VII—unknown ..	0	17	23	40
	6	134	156	296

The Racial Incidence of Anaemia

The Indians, both Southern and Northern, show a higher incidence than the Chinese or Malays, and also a higher proportion show a megaloblastic type of anaemia. This is shown in Table II.

The Prevalence of Iron Deficiency

Tasker (1955) has shown by serum iron studies, and by staining marrow smears for

TABLE II

Racial Incidence of Severe Anaemia. Showing the Total Numbers Admitted, and as a Percentage of the Total Deliveries of that Race, and the Proportion with a Megaloblastic Anaemia

	Total Number Admitted	Number Admitted as a Percentage of Total Deliveries	Percentage with a Megaloblastic Anaemia
South Indian	219	12	49 (25)
North Indian	15	8	64 (26)
Chinese ..	47	2	30 (18)
Malay ..	12	4	10 (9)

Figures in brackets show those with a grossly megaloblastic marrow, the remainder signifies an intermediate megaloblastic marrow.

siderocytes, that iron deficiency is almost invariably present in patients with nutritional anaemia as encountered in Malaya. Upon this basic deficiency may be superimposed additional types of anaemia, of which that associated with a megaloblastic marrow is the most important and common. Indeed, iron deficiency can be so severe as to prevent the development of the megaloblastic component until iron has been given. Thus, the patient may present a microcytic hypochromic normoblastic anaemia, having a very low serum iron level, and no siderocytes in the marrow; yet with iron therapy there is no response and a later marrow smear will show a grossly megaloblastic picture. Figure 1 illustrates a typical instance of this sequence of events.

Some of the patients with megaloblastic anaemia showed a vitamin B_{12} deficiency as demonstrated by serum assays.

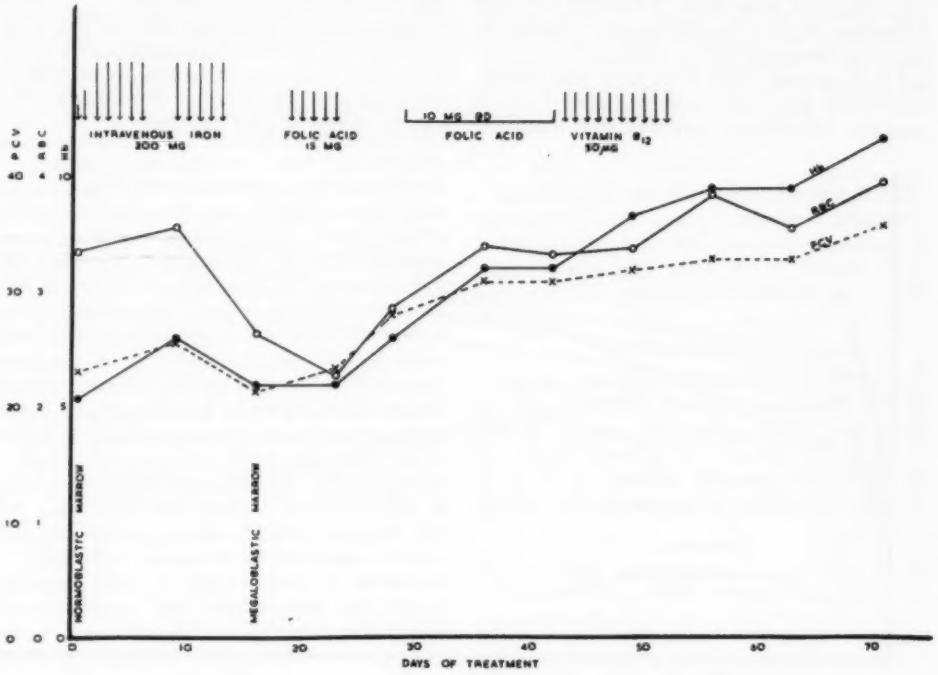

FIG. 1

Illustrating the progress of a patient whose anaemia changed from a normoblastic to a megaloblastic type with iron treatment. Aged 26, para-4, 28-weeks pregnant.

TABLE III

Showing the Serum Vitamin B_{12} Concentrations (μμg./ml.) Found in 40 Patients with Severe Megaloblastic Anaemia of Pregnancy

(Normal 100–720 μμg./ml.)

	Serum Vitamin B_{12}			
	Less than 120 μμg./ml.	121–240	241–480	481 and above
Indians ..	6	9	12	4
Chinese ..	1	2	2	–
Sikhs ..	1	1	2	–

TREATMENT

Because of this prevalent iron deficiency, all patients were treated with iron. This was given either as ferrous sulphate, 18 grains daily by mouth, or as intravenous saccharated iron oxide 50 mg., then 100 mg. and thereafter 200 mg. daily to a total dose of between 1·5 and 2·0 grams. Most of the patients were discharged when the haemoglobin had risen to between 10 and 11 g. per cent. Apart from some local venous thrombosis and pain after accidental extravasation, intravenous iron was well tolerated, excepting for one batch used during 1953 which caused a high incidence of toxic reactions, some severe, one of which resulted in death.

Follow up studies over about one year showed, under these conditions of treatment, the superiority of intravenous iron in maintaining the haemoglobin level after cessation of treatment. A few examples are shown in Figure 2 and the curves here also give an indication of the approximate proportion of successes and failures.

In treating the megaloblastic element of the anaemia, folic acid is at present considered to be the treatment of choice (Wilkinson, 1948; Davidson, Girdwood and Clark, 1948; Das Gupta, Chatterjea and Mathen, 1949). We have used this orally, in a dosage of 20 mg. daily for 10 days, or subcutaneously 15 mg. daily for 5 days. The parenteral scheme does not appear to offer any advantage over the oral.

Most patients responded well to this treatment, but a proportion responded poorly or not at all. This refractory state appears to hold no relationship to the duration of pregnancy, but may be related to liver damage.

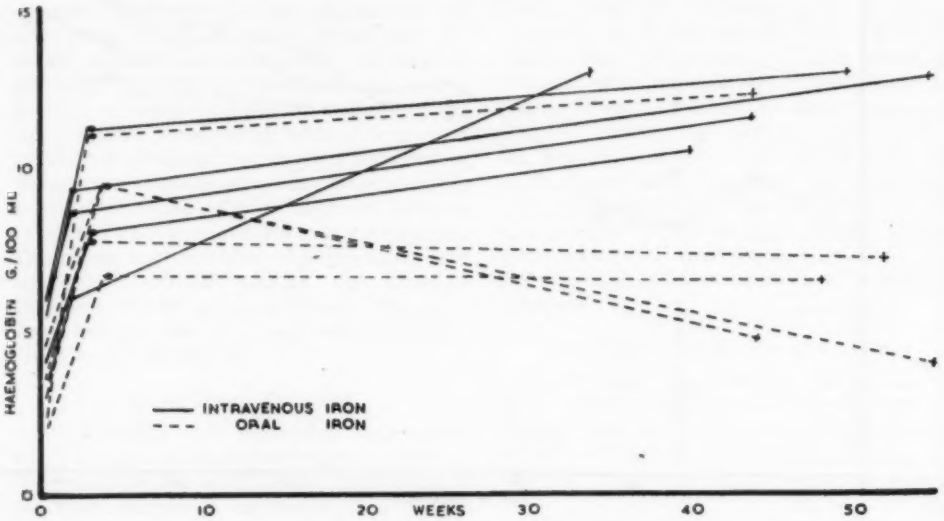

FIG. 2

Illustrating the type of follow-up results obtained after oral and intravenous iron therapy. The black circle represents the time of discharge from hospital and end of treatment.

As might be expected, some of those with a low serum vitamin B_{12} level showed a good response to treatment with 50 μg. daily for 10 days. Eleven of 20 patients so treated gave a good response. Writers from Europe and North America find vitamin B_{12} deficiency in pregnancy megaloblastic anaemia to be rare, at least as judged by response to treatment (Miller and Studdert, 1942; Holly, 1951; Thompson and Ungley, 1951; Scott, 1954). Yet those writing from India find that vitamin B_{12} not uncommonly has a therapeutic effect (Patel and Kocher, 1950; Chaudhuri, 1951; Das Gupta, 1953). The proportion of patients with a low serum vitamin B_{12} level encountered in Malaya does not appear to be greater than that found in England (Mollin and Ross, 1952, 1954). But the proportion of patients who responded to vitamin B_{12} therapy in Malaya was greater than in England for we have found that some of the patients with a serum vitamin B_{12} level at the lower limits of normal responded favourably to treatment.

Blood transfusion was given during 1954 to 14 patients, 11 because of post-partum haemorrhage. Many patients went through labour with a haemoglobin of between 3 and 5 g. per cent and no trouble was encountered, although blood was held in reserve in case of haemorrhage. Care was taken to prevent blood loss during delivery and intravenous ergometrine 1 mg. was given with the birth of the head of the baby. We feel with increasing confidence that blood transfusion has a limited indication in these patients, because heart failure is readily precipitated in these severely anaemic patients by even a small transfusion, so that we tend to conserve our limited stocks of blood to combat actual haemorrhage.

During the year 2 patients died. One had a severe megaloblastic anaemia (haemoglobin 3·8 g. per cent) and pyrexia, and who died 10 days after delivery in heart failure. The other was a patient with megaloblastic anaemia and liver damage, who, 6 hours after a premature delivery, lapsed into hepatic coma and died. A post-mortem liver biopsy showed acute necrosis of the liver cells.

Discussion

This brief survey of our experiences reveals some points of interest when compared with experience in temperate climates. Of particular note was the higher incidence of anaemia as a whole, of which a high proportion was megaloblastic; of the latter, a greater proportion in Malaya was wholly or partially sensitive to vitamin B_{12} treatment. This is particularly marked with the Indians, who suffer relatively badly. Including the experience found among non-pregnant women and men, it was found that the Northern Indian shows a higher incidence of megaloblastic anaemia than even the Southern Indian. A higher proportion of the former were vitamin B_{12} deficient as judged by serum levels.

The Southern Indian has a poor diet, eating little food of animal origin and subsisting mainly on rice and non-leafy vegetables, the whole mixed into a repetitive and monotonous curry. The Northern Indian, usually a vegetarian, subsists on unleavened bread, rice, milk, green pulses, a little vegetable and rarely any other animal foodstuff. In contrast the Chinese tend to eat a more balanced diet, more comparable with that consumed by Europeans. Only when driven to the extremes of poverty is the normal balance of their food intake upset.

Summary

Experiences from the investigation and treatment of the many severe anaemias of pregnancy in Malaya are described. Particular reference is made to the high incidence of megaloblastic anaemia. The results of treatment are briefly discussed.

Acknowledgments

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CARCINOMA OF THE BODY OF THE UTERUS AND ITS RELATIONSHIP TO ENDOMETRIAL HYPERPLASIA

A Histological Study

BY

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THE histological appearances of 81 cases of carcinoma of the body of the uterus have been studied chiefly with a view to investigating the frequency of association and the relationship between carcinoma and hyperplasia of the endometrium, and a possible mode of evolution of the malignant process in some instances. This group of cases was admitted to St. Thomas' Hospital between 31st January, 1943 and 31st March, 1952. It is unfortunate that, owing to the war, the pathological investigations undertaken during the early part of this period are not so extensive as otherwise they might have been.

In view of the widely differing histological appearances it is thought desirable to discuss the variations in cell type, the invasion of the myometrium, the presence or absence of secretion and other features under appropriate headings.

TYPE OF CELL

The systematic examination of sections of curettings or of the uterine wall after hysterectomy shows that in adenocarcinoma of the uterus the type of cell may vary from a short columnar form, as found in a few cases, passing through columnar cells of intermediate size to a tall pale distinctive type which is a characteristic finding of a large group.

In a small number of cases (7 in this series) the growth is characterized by short columnar cells which stain deeply and call to mind the glandular epithelium of the normal early post-menstrual endometrium (Fig. 1). In some cases only a portion of the curettings removed for diagnosis is malignant, so that without thorough curettage the correct diagnosis might be missed. The macroscopic examination of the uterus after removal frequently shows only a small papilliferous growth situated perhaps at one of the cornua. The remainder of the endometrium may be innocent and perhaps atrophic.

In the more differentiated adenocarcinomas, however, the type of cell is much taller and in 38 cases of this series it shows peculiarly distinctive features. Many of the glands, in some cases a large majority, are lined with tall cylindrical cells which stain less intensely and give a pale pink colour with haematoxylin and eosin. The cells which are closely packed together are arranged in palisade fashion and show vesicular nuclei situated at different levels in the glandular epithelium (Fig. 2). They bear a resemblance to the tall glandular epithelial cells sometimes found in cases of cystic hyperplasia of the endometrium.

In the 12 cases of adenocarcinoma in which the columnar cells are of intermediate size it is possible that in some instances these cells represent a later stage in the dedifferentiation of the tall pale cells. They stain more intensely and are not so uniform in shape and size.

In 22 cases histological examination showed a high grade of malignancy. The appearances are so atypical that no resemblance to the glandular cells of the normal endometrium can be seen. Considerable variations in shape and size are shown and in some cases there is a definite reversion to a small round type (Fig. 3).

Two cases of pure squamous-cell carcinoma were found in this series.

Appearances of the Co-existent Endometrium

Among these 81 cases of carcinoma of the body there were 22 in which the co-existent innocent endometrium was available for study. Of these, 5 were normal or atrophic and 17 showed cystic hyperplasia. Twelve in the latter group were associated with the presence of the tall pale glandular epithelial cells described above. It will be appreciated that in many cases the malignant process is so advanced when first examined that any benign pre-existing condition will have been replaced by carcinoma so that the above figures are probably an understatement.

The Changing Picture of Hyperplasia of the Endometrium

Hyperplasia of the endometrium has been considered to be due to the action of the oestrogenic hormone. Cytological examination of the vaginal smear, along with histological examination of curettings from the uterus, has shown that oestrogenic hyperactivity, perhaps associated with endometrial hyperplasia, may show atypical epithelial proliferation. These changes, about to be described, have been found in a significant number of the present series.

Endometrial polyps, which may be rightly regarded as a localized form of endometrial hyperplasia, and with which they are often associated, have been observed by a number of authors to precede the development of carcinoma. In this series polyps were found to co-exist in 2 cases; one showed multiple tumours, the other a solitary one. The histological structure of the solitary polyp is shown in Figures 4 and 5. Sections show the appearances of cystic hyperplasia but, at the upper left-hand portion, there is an area of epithelial proliferation with atypical, closely-packed glands lined with tall epithelial cells, representing an early change in the direction of carcinoma.

In most cases, however, the endometrial hyperplasia associated with carcinoma of the body is widespread and may also show atypical epithelial changes. There may be small, localized areas in the endometrium showing complicated and bizarre glandular patterns. The gland lumina may, in some cases, be filled with proliferated epithelial cells. Usually, however, these changes are diffuse. The glands, greatly increased in number, perhaps formed of the tall pale epithelial cells, may be crowded together in haphazard fashion with little intervening stroma; large and prominent glandular invaginations may be seen; adenomatous proliferation of the glandular epithelium with the formation of papillary buds projecting into the lumen may be found. These appearances may be present together in the same endometrium (Fig. 6). The transition from areas of cystic hyperplasia to those of atypical epithelial proliferation or of actual carcinoma is often abrupt (Fig. 7).

The individual gland cells may become quite abnormal in appearance showing hyperchromatism, many mitotic figures, variations in shape and size. In some cases the appearances are so atypical that opinions differ as to whether they should be regarded as malignant or not. In other cases, however, in the same curettings different appearances may be seen, passing from an endometrium containing many glands of normal pattern, through an endometrium showing typical cystic hyperplasia with adenomatous proliferation of the glandular epithelium, to a condition of frank papillary carcinoma (Fig. 8 (*a*), (*b*), and (*c*)).

Invasion

The question of invasion of the uterine muscle may be difficult to determine. It is impracticable to cut and examine sections of all tissue involved in every case, so that in some invasion may be missed for this reason alone. Nevertheless, it is well known that many cases of carcinoma of the body of the uterus remain localized to the endometrium for a considerable period and in some described here normal glands from the deep part of the mucosa may be seen in between the atypical glands close to the uterine muscle (see Fig. 6). The difficulty is increased by the fact that endometrial hyperplasia in its simple form is frequently accompanied by a certain degree of adenomyosis.

Secretory Activity

In a number of cases examination of the haematoxylin and eosin sections has shown apparent secretory activity in the carcinomatous

FIG. 2
An adenocarcinoma formed of tall pale epithelial cells with nuclear appearances as described in the text. ×100.

FIG. 1
An adenocarcinoma of low columnar cell type. ×120.

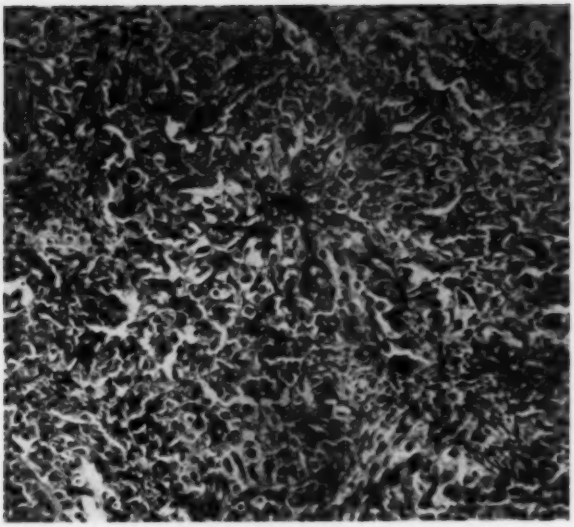

FIG. 3

An endometrial carcinoma of anaplastic type. ×112.

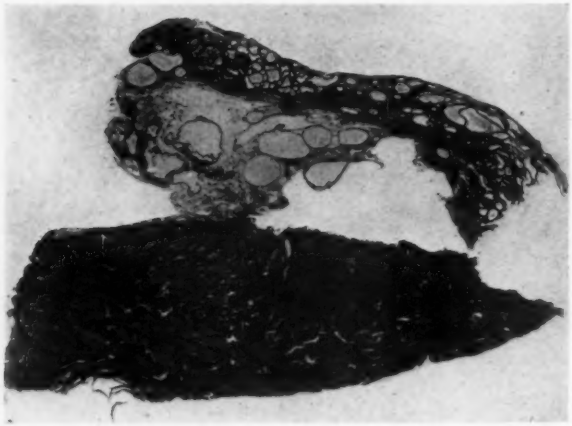

FIG. 4

An endometrial polyp with cystic glands. At the top left-hand corner is a densely stained area which is shown in higher magnification in the next figure. ×4.

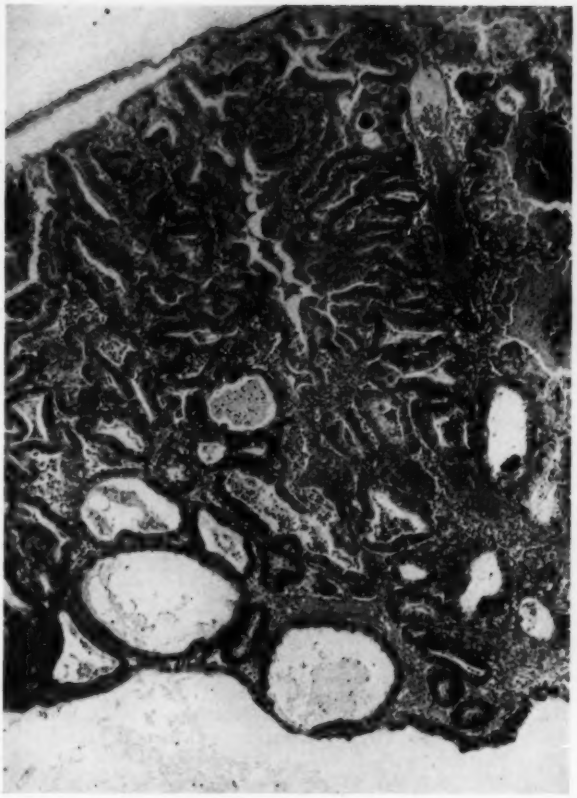

FIG. 5

The area of early carcinomatous change in the densely stained area seen in Figure 4.

FIG. 6

The superficial part of the endometrium shows diffuse atypical proliferation of the glandular epithelium. The deeper part consists of glands formed by tall pale epithelial cells. The arrow indicates an abrupt change in the character of the epithelium. ×30.

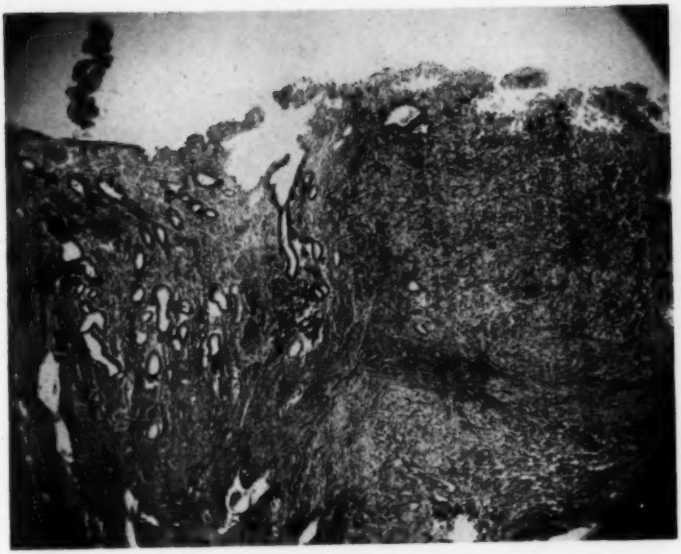

FIG. 7

An abrupt change from cystic hyperplasia to anaplastic carcinoma. ×30.

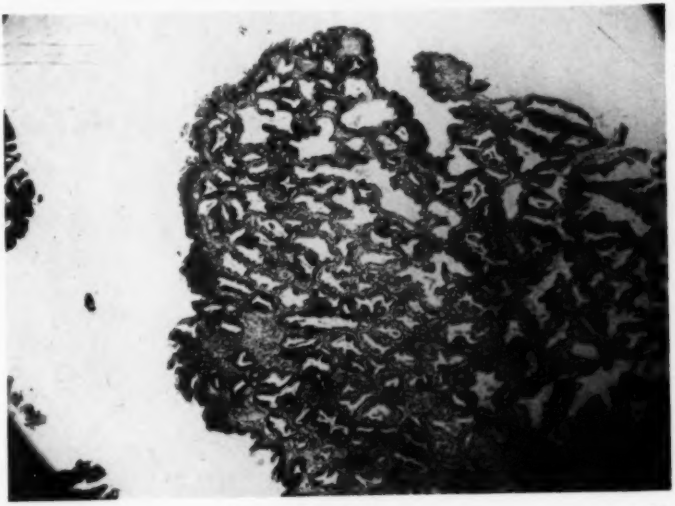

FIG. 8(*a*) ×30

FIG. 8(*b*) ×28

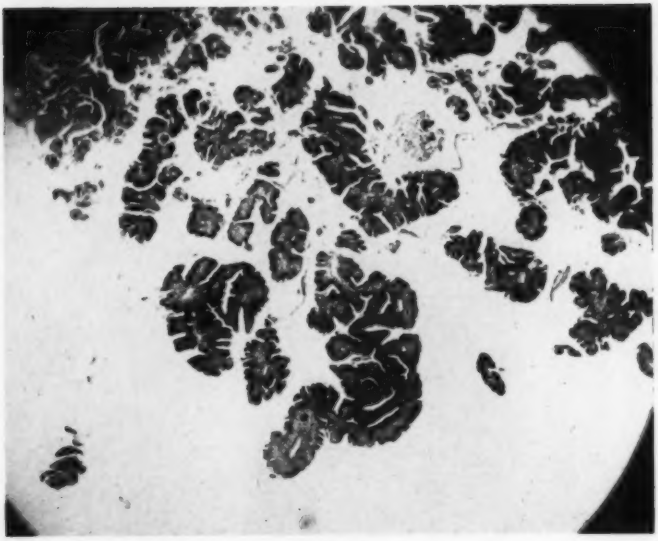

FIG. 8(*c*) ×28

FIG. 8(*a*), (*b*) and (*c*)

All three sections from different parts of the same endometrium showing the normal pre-menstrual appearances, cystic glandular hyperplasia with adenomatous proliferation, and papillary carcinoma respectively.

J.B.

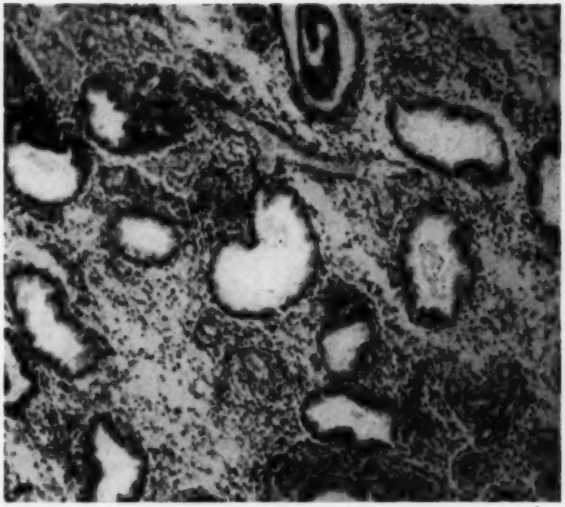

FIG. 9(*a*) ×112

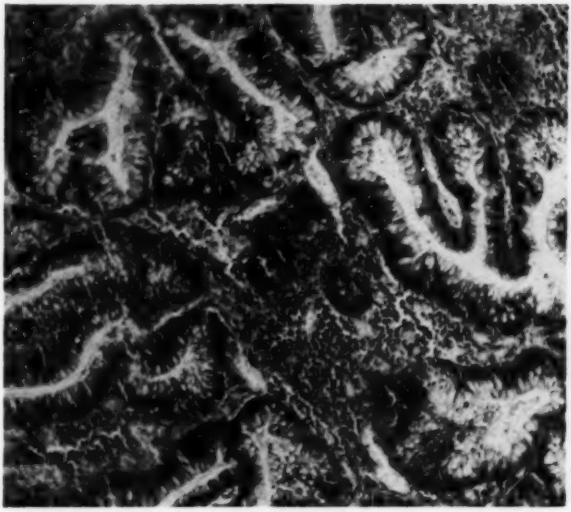

FIG. 9(*b*) ×112

FIG. 9(*a*) and (*b*)

Both sections are from the same endometrium.
(*a*) Shows a normal secretory mucosa.
(*b*) Is an area of malignant tissue with marked secretory activity.

J.B.

tissue. Preparations stained by mucicarmine, by carmine for glycogen, and by Schiff's periodic method have been used for confirmation. In some cases the secretory activity is minimal; in 10, however, the activity is pronounced. When normal endometrium and carcinomatous tissue from the same uterus have been examined, both have shown secretory activity but the malignant tissue in greater degree (Fig. 9 (*a*) and (*b*)). Four of the 10 neoplasms showing abundant secretion have been associated with cystic hyperplasia and it is known that 2 of those patients had been taking oestrogen for a considerable period.

Squamous Metaplasia

Squamous metaplasia has been found in 18 of the 81 carcinomas in this series and this change occurred with all grades of malignancy. In one case it was so pronounced as to justify the description "adenoacanthoma".

The Ovaries in Carcinoma of the Endometrium

Histological examination of the ovaries was possible in 44 cases. In 36 there was no evidence of follicular activity except that in 6 of these one or two germinal retention cysts were found. In 4 cases typical follicular cysts were present. The youngest of these was in a woman of 21 years, in whom four or five cysts, lined by two or three layers of granulosa cells, were discovered in each ovary. In one patient there were two lutein cysts in one ovary; in another patient, two theca-lutein cysts. Pseudo-mucinous cystadenoma of the ovary occurred once in this series of cases but granulosa or theca cell tumour was not found. Stromal hyperplasia, as described by a number of authors, was considered to be present in more than half of the cases. Ovarian metastasis was found on one occasion only when there was a small malignant deposit on the surface of one ovary. These findings in the ovaries correspond closely with those found in cases of endometrial carcinoma by other authors (Wohl *et al.*, 1948; Novak and Mohler, 1953).

Discussion

The question of a causal relationship between hyperplasia of the endometrium and carcinoma has been a subject of controversy for many years. Meyer (1923) stated that "the morphological distinction between hyperplasia and carcinoma is dependent upon differences of degree only and that there are cases which are practically transitional". Ewing (1928) wrote that, "in a series of cases of hypertrophic endometritis, every gradation may be observed from normal glands to those of adenoma malignum". Other authors, for example Shaw (1929), denied that any relationship existed between the two conditions. Taylor (1932) considered that there was a relationship and that from the morphological standpoint it depended upon:

(1) Morphological similarity, certain types of hyperplasia showing close resemblance to certain differentiated carcinomas.

(2) The tendency to invasion of the uterine muscle in both conditions.

(3) The transformation of hyperplasia to carcinoma as observed in successive curettings in the same patient.

(4) The association of both conditions in the same uterus.

Novak and Yui (1936) found associated hyperplasia in 39 per cent of 64 cases of carcinoma of the uterus in which sections of co-existing endometrium were available for examination. Of 32 cases of cancer of the body of the uterus, in which it was possible to examine the endometrium from one to twenty-three years before invasive carcinoma was diagnosed, Hertig and Sommers (1949) found 17 examples of cystic hyperplasia, the highest incidence being 6 to 13 years previously. They considered that cystic hyperplasia tended to be a remote rather than an immediate forerunner of carcinoma. All this evidence suggests that hyperoestrinism is an important underlying factor. It would be expected therefore that granulosa cell tumours of the ovary which are so frequently associated with endometrial hyperplasia should be found in a significant number of cases with adenocarcinoma, and several authors have reported such an occurrence. It is considered that the association of endometrial cancer in cases of feminizing oestrogen tumours is too frequent for it merely to be a coincidence. Some authorities, however, believe that the association is purely fortuitous and without significance.

TeLinde, Jones and Galvin (1953) believe that there is the strong suggestion that many lesions previously diagnosed as "atypical hyperplasia", "adenomatous hyperplasia" and "proliferative hyperplasia" are in fact carcinoma. This opinion is based upon the fact that these lesions are frequently found in the same endometrium with advanced carcinoma and may also show histological transition to the more malignant appearing ones. They consider that endometrial carcinoma may be preceded by similar hyperplastic lesions for several years.

Gusberg (1947) described a pattern of adenomatous hyperplasia of the endometrium bearing a constant relation to oestrogen stimulation in both benign and malignant tissues. He found this pattern to occur in four groups of cases:

(i) Endometrial hyperplasia produced by granulosa-cell tumours.
(ii) Endometrial hyperplasia produced by prolonged oestrogen administration.
(iii) Endometrial carcinoma arising in patients receiving prolonged oestrogen administration.
(iv) Endometrial patterns in patients with repeated episodes of functional bleeding.

In the present series of 81 cases of carcinoma of the endometrium, 17 showed a co-existent hyperplasia of the endometrium, including 2 of 4 cases following oestrogen administration. In the majority of cases there is no evidence to show how long the hyperplasia had existed. No case of granulosa cell tumour has been found in this series. The presence of the tall pale eosinophil glandular cells constitutes a striking picture in 38 of the cases. It would appear that the formation of these curiously distinctive glands represents a definite stage in the evolution of a certain number of cases of carcinoma of the endometrium. Hertig and Sommers (1949) have described the condition of carcinoma *in situ* occurring in the endometrium, and noted 64 cases in the period 1934 to 1948, during which time 275 cases of invasive adenocarcinoma were diagnosed. They consider that carcinoma *in situ* may exist in hyperplastic or atrophic endometria or in endometrial polyps. They describe these areas as being formed of large cells with abundant clear eosinophilic cytoplasm and pale nuclei, obviously identical with the cells observed in this series. Hertig and Sommers found that 6 of these 64 cases of carcinoma *in situ* proceeded to develop invasive cancer one to eleven years after the diagnosis of carcinoma *in situ* was made. Four cases had carcinoma *in situ* and invasive endometrial cancer side by side. The development of carcinoma *in situ* in endometrial polyps occurred in 14 of the 64 cases.

As stated above, 38 of the 81 cases in the present series were characterized by the presence of the tall pale eosinophil glands. In some the whole of the neoplasm was formed by this type of tissue. In others this was not the case. At the base a few of the normal basal glands lying close to the uterine muscle might still be persisting. The tall pale glands were observed in some cases to be directly continuous with glands showing adenomatous proliferation and atypical cellular changes—a transition to a more malignant type of tissue. This change may be shown in the more superficial part of the endometrium, as illustrated in Figure 6. In other cases areas of marked secretory activity were found adjacent. Of these 38 cases, 18 appeared to show definite invasion and the tall pale eosinophil glands unaccompanied by stroma were found penetrating the uterine muscle.

The question arises as to the length of time required for the development of carcinoma in a case of endometrial hyperplasia. More information is needed on this subject but it would appear that in most cases a considerable period is necessary. A patient, aged 32, was admitted in 1941 under the care of Mr. Kenneth Bowes for menorrhagia following childbirth two years previously. Cystic hyperplasia of the endometrium was found. During the ensuing twelve years she continued to have heavy losses necessitating oestrogen for control. Further curettings in 1947 and 1951 showed typical cystic hyperplasia. In 1953 another curettage revealed endometrial carcinoma with invasion of the myometrium.

Summary

Eighty-one cases of endometrial carcinoma have been studied by the examination of curettings and/or of sections of the uterine body. In 17 of these a co-existent cystic hyperplasia of the endometrium was found. Certain cell types of

carcinoma have been distinguished and attention drawn to a large and distinctive group characterized by tall pale eosinophil glandular cells which have been previously reported by one or two authors. In 12 of the 17 cases this curious glandular epithelium was present. Evidence has been presented of transitional histological changes in the glandular epithelium, which may be formed by these tall pale cells, in the development of malignancy. In some cases the line of demarcation between innocent and malignant tissue has been abrupt. Well-marked secretory glandular activity has been observed in 10 cases of endometrial carcinoma.

I am indebted to the gynaecological staff of St. Thomas' Hospital under whose care these cases were admitted.

I wish to thank Mr. R. B. Rickford who collected the material for the purposes of clinical analysis and Mr. Kenneth Bowes for the kindly interest shown and valuable advice given in the preparation of this paper.

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CYST OF SKENE'S GLAND

BY

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IN the formation of the female uro-genital tract, the urethra and its glands develop from the uro-genital sinus and the vagina forms from the Müllerian (or Paramesonephric) Duct. Skene's glands are specialized para-urethral glands equivalent to the prostate gland in the male, and found one on each side of the external urinary meatus, with a single duct from each gland opening into the side of the urethral orifice. Remnants of the Wolffian (or Mesonephric) Duct are occasionally found alongside the Müllerian system and called Gaertner's Duct.

While cysts of Gaertner's duct are fairly common, most authorities agree that cysts of Skene's gland are very rarely seen (Shaw, 1954) and few cases have been reported. In the records of St. Thomas' Hospital since 1937 I could not find a true case of a cyst of this gland. Legault of Montreal described a case in a communication to the Montreal Surgical Society in 1946. His patient was a married woman of 36 with 5 children, the youngest being 2 years old. She had had constitutional symptoms with some frequency of micturition for 2 years and was admitted to hospital with a recent onset of pain on micturition and a pyrexia around 99° F. (37·2° C.), which lasted for 3 days. The cyst was the size of a large olive and contained greeny yellow sebaceous material which unfortunately was not cultured. The cyst was easily excised surgically.

This author discusses fully the differential diagnosis from urethral abscess, polyp, carcinoma, urethral prolapse, diverticulum, calculus and herniation into the urethra of a cystic dilatation of the lower end of the ureter. A cyst of the gland of Skene shows as a small swelling about ½ to 1 inch (1·25 to 2·5 cm.) in diameter, in or just beside the midline between the mouth of the external urinary meatus and the vaginal opening, producing a bulging of the anterior vaginal wall. Martius (1953) remarks on the spherical shape produced at the end of the urethra and Nel (1955), in an article on urethral diverticula, points out that the latter condition shows as a pouch. In the main the cyst is symptomless until infection occurs in it and it is apparent that no difficulty in diagnosis should be found.

Treatment by diathermy cautery or surgical excision is easy and recommended, and the prognosis is good as the cysts do not recur (Legault, 1946; Crossen and Crossen, 1938).

CASE REPORT

The patient was an intelligent married woman of 30 years with one small child. Her past history had been very healthy and the cyst was discovered on routine pelvic examination in April, 1954 at the 36th week of pregnancy. The cyst had caused no symptoms and the patient was unaware of its presence. It was slightly oval, about ¾ by ½ inch (1 by 1·25 cm.) lying in the long axis of the midline of the vagina immediately below the external urinary meatus and causing a slight pouting of that meatus. It was not tender, there was no discharge and there was no evidence of infection.

The cyst gave no trouble during the pregnancy or at the delivery, which was spontaneous, in May, 1954. The baby weighed 7 pounds 5½ ounces (3·3 Kg.). The puerperium in hospital was uneventful, there being no pyrexia or abnormal micturition, and breast feeding was established. The baby, however, developed a paronychia when about a fortnight old, due to a *Staphylococcus aureus*, and this in turn infected the palate and lachrymal apparatus. Breast feeding became technically difficult and only the left breast could be used. An abscess now developed in this breast and culture of the pus showed a similar *Staph. aureus*. At about this time, *Staph. aureus* infection occurred in the vulval skin of the mother.

At the postnatal examination the patient reported that she had had occasional dysuria, a sense of irritation at the urinary meatus and slight discharge. She was now aware of the cyst and felt herself that it had become infected.

A swab of the discharge from it grew *Staph. aureus* which was resistant to all the antibiotics except Aureomycin. At that time, in view of all the circumstances, it was decided to treat the cyst conservatively.

During the next few months the cyst varied between its former size and the size of a small plum, with intermittent discharge from it. There were one or two severe exacerbations of the infection which were treated by Aureomycin, but the details of these are not known. Although there were no other symptoms, the patient was advised to have the cyst excised. At operation, in July, 1955, the cyst was about $\frac{1}{2}$ inch (1·25 cm.) in diameter and was freely discharging. Removal of the cyst through an incision in the anterior vaginal wall was accomplished without much difficulty and the post-operative period was uneventful. An indwelling catheter was inserted for 36 hours and a short course of Sulphatriad was given for the first 4 days. Culture of the discharge grew only an atypical *Bacterium coli* and the histology of the cyst revealed nothing which could show its origin.

Comment

Legault (1946) in his paper states that urethral cysts in the female more often occur in multiparous women or following infection. Novak and Novak (1952) and MacLeod and Read (1955) mention that the gonococcus is the usual associated organism.

This case is of interest in that it illustrates the points useful in diagnosis and in the lack of symptoms until infection occurred. The causative organism was unusual and the method of spread of the original staphylococcus was easily followed.

I wish to thank Professor A. S. Duncan of the Department of Obstetrics and Gynaecology, Cardiff Royal Infirmary, for his most helpful notes on the earlier history of this case, and Kenneth Bowes, Esq., of St. Thomas' Hospital, for his encouragement and advice.

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EARLY OPERATIVE INTERFERENCE IN AFIBRINOGENAEMIA OF PREGNANCY

BY

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IN this country interest in the condition of incoagulability of the blood following premature detachment of the placenta has recently been aroused by the papers of Moore (1954), and of Barnett and Cussen (1954), and by the editorial comment in the *British Medical Journal* (1954). O'Donel Browne (1952) and Tenney (1954) have recently recommended early Caesarean section, and this is a recommendation that has been revived many times since first suggested by Pinard in 1898.

The following case is presented because immediate Caesarean section was undertaken successfully from the maternal outcome, and because it demonstrates the ability of the patient to recover without the parenteral administration of fibrinogen, if the uterus is evacuated without delay.

CASE HISTORY

Mrs. K., age 31.

Previous Obstetric History

1947—Full-time, forceps delivery of a female infant 8 pounds 12 ounces in weight. Alive and well.

1949—Full-time spontaneous delivery of twins, male and female, weighing respectively 2 pounds and 4 pounds; both alive and well.

1951—Full-time delivery of male infant, 7 pounds.

On the 20th August, 1954, the patient first attended her general practitioner, Dr. Ada Dudack-Bentley, to whom we are indebted for her antenatal notes. Mrs. K. was then approximately 18-weeks pregnant and she complained of a brown discharge.

On 21st September, 1954, the blood pressure was 120/80 and the urine normal; but the patient complained that she had seen "a streak of blood".

On 12th November, 1954—B.P. 120/80. The patient complained of cramps down the thighs. There was no bleeding nor had there been any when she had been seen in October, 1954.

On 16th December, 1954 Dr. Bentley was called to the patient's house where she found the patient lying in a pool of blood and she estimated that a loss of between 2–3 pints had occurred.

The patient was immediately transferred to hospital.

On arrival at Oldchurch Hospital soon after 2 p.m. she told the house surgeon that she had not felt well during the previous night. At 10.30 a.m. she had suddenly felt a "heaviness"; then pains quite unlike labour pains. Suddenly something "burst", which she was certain was not "her waters". She found that she had begun to lose bright red blood. She fainted, but after some time managed to call a neighbour.

At the time the patient was admitted she was still bleeding freely and soon the sheets on the admission ward bed were soaked. The pulse was weak at a rate of about 100. The patient was pale and shocked. The blood pressure was 85/50 mm. Hg.

Through a vein-puncture blood was taken for cross-matching and "Plasmosan" transfusion was started. Morphia gr. ¼ was given intramuscularly. After ½ hour the transfusion needle came out of the arm because the patient moved. About ¾ pint of Plasmosan had then been given.

It was thought that the foetal heart could be heard at 160 beats per minute. The mother's pulse rate was 80/min. and it was later realized that the foetal heart that had been "heard" was the transmission of the mother's first and second aortic sounds through her tense uterus.

It was noted that the blood taken for cross-matching did not clot. The decision was made to transfer the patient to the theatre for examination under anaesthetic, and Caesarean section, if the cervix was not fully or almost fully dilated.

At 3.05 p.m. under a general anaesthetic (Dr. Kinnish)

the foetal heart could not be heard. The foetal head was high above the brim of the pelvis in the right iliac fossa. The placenta was felt through a cervical os that was only two fingers dilated. The placenta was clearly free and a tentative diagnosis of "prolapsus placentae" was made.

The decision to carry out a Caesarean section was made primarily because it was considered that at the rate at which the patient was losing blood her life could not be saved unless the area from which she was bleeding was rapidly lessened. The only way to achieve this rapid diminution in size of the utero-placental site was thought to be by Caesarean section. We were determined to carry out Caesarean hysterectomy only if the uterus failed to contract, because we did not feel that the area from which haemorrhage could occur would thus be diminished appreciably.

At the back of our minds to encourage us to proceed to Caesarean section we had O'Donel Browne's paper advocating Caesarean section in ante-partum haemorrhage in the interests of the mother even more than that of the child.

Rupturing the membranes in the presence of a prolapsed placenta would, of course, have been possible, but not easy. There was also the factor of non-engagement of the foetal presenting part to sway us to performing a Caesarean section.

So a lower segment Caesarean section was rapidly performed with transverse incision into the uterus, which appeared extensively "Couvelaire". A stillborn early macerated female infant weighing 6 pounds 10 ounces was delivered after the intact membranes had been ruptured. The placenta was lying free in the uterus. An interesting finding was that the liquor was clear and not at all discoloured. There was blood free in the uterus, but the placenta itself was quite smooth. The incision in the uterus was repaired with continuous catgut in 3 layers. Meanwhile intravenous ergometrine 0·5 mg. was given.

As oozing from the uterine wound continued in spite of good apposition of the wound edges, a corrugated rubber drain was inserted beneath the utero-vesical peritoneum and brought out to the lower end of the abdominal wound to ensure that there would be no added shock from intra- or retro-peritoneal blood collection.

The abdomen was rapidly closed in layers including a subcuticular nylon stitch and three nylon deep tension stitches.

At the culmination of operation at 3.30 p.m. a cut down transfusion into the left leg was made and later a second cut down into the right arm was made. The pulse now was very weak indeed and the rate 110 per minute.

Oozing from the interperitoneal drain continued as it did from the vagina. There was no evidence of any blood clotting, either in blood from the wound or from the vagina. A further intravenous dose of ergometrine 0·5 mg. was given. It was considered that the rate of combined loss approximated but did not exceed the rate of replacement at 4.30 p.m. By this time 2 pints Plasmosan and ½ pint of stored blood had been given.

The rate of transfusion was still unintentionally slow because the blood could not be made to move faster than about 40 drops per minute in either drip. When, however, positive pressure was applied indirectly by Higginson's syringe to the arm transfusion at 5.15 p.m. the rate of transfusion was raised to 100 drops/minute. By 5.45 p.m. improvement in the patient's general condition was for the first time obvious.

By 6 p.m., however, and before any fresh blood had been given and when only 1½ pints of 2-weeks-old stored blood had been administered the oozing had ceased and a clot had been passed per vaginam. A steady improvement in the general condition had resulted by 9 p.m. when the blood pressure was 100/60. The following morning the blood pressure was 110/70 mm. Hg and it stayed at this level until the patient left hospital on the 16th post-operative day.

During the time the Caesarean section was being carried out and the resuscitative measures were being performed the case presented itself to the laboratory as follows:

Blood received for cross-matching at 2.30 p.m. failed to clot.

A further specimen was taken at 2.45 p.m. to guard against the possibility of the contaminating presence of anticoagulants, and it also failed to clot.

The following tests were performed:

(1) A third specimen of the patient's blood failed to form any clot whatever after incubation at 37° C. for twelve hours.

(2) A specimen was taken for electrophoresis. (This later showed no fibrinogen band.)

(3) The blood failed to clot when thrombin was added.

(4) The plasma from a patient on anticoagulant therapy (Dindevan) was obtained. This gave a "prothrombin time" (Quick method) of 25 seconds. Equal parts of the plasma and of our patient's plasma were mixed. A "prothrombin" time performed on the mixture gave a normal reading of 15 seconds. From these tests it was concluded that the patient's fibrinogen level was extremely low while the prothrombin and/or factor VII level were within normal limits. It also seemed to indicate the absence of circulating anticoagulants acting after the stage of generation of thromboplastin.

(5) A normal clot incubated for 12 hours in 5 times its volume of the patient's plasma showed no change to simple observation.

From this it appeared that there was no gross fibrinolytic activity, although it is appreciated that a more delicate test is necessary to demonstrate this phenomenon at its expected level.

From these findings, and from the obstetric history and opinion, it was clear that the patient was suffering from acquired hypofibrinogenaemia of pregnancy. In view of the obstetric decision to operate, and bearing in mind the recent reports of the near-infallibility of parenteral fibrinogen in these cases, it was decided to attempt to "cover" the immediate operation by cross-matching four pints of stored blood and by sending for two emergency donors for fresh blood, while at the same time an urgent appeal was made for the delivery of a supply of fibrinogen. The appeal was met by the National Transfusion Service Edgware Centre to whom we are indebted for kindness and co-operation. At 5.40 p.m. the fibrinogen had become available, and at 5.45 p.m. it was decided to perform a clot observation as a control before administration. A small clot formed in 2 minutes. It had disappeared again in about 20 minutes. It was also observed clinically at this time that oozing had ceased from the operation site, and a clot of blood was passed vaginally which at first disconcerted the nursing staff but delighted the obstetric surgeon.

At 6.45 p.m. a rather better clot formed in the test tube on repeating the test, and at 7.30 p.m. a still better one which remained stable for some hours. In view of these findings and the improvement in the patient's condition no concentrated fibrinogen was administered at any time. During the whole operation and postoperative period only 4 pints of blood were given. Up to the time of the appearance of the first clot 1½ pints of 2-weeks-old stored blood were administered. Between this time and the next morning the remainder of the second pint of old blood and 2 pints of fresh blood were given, making 2 pints of old and 2 pints of new blood in all.

At 10.30 a.m. the next day, blood taken clotted quite normally. Fibrinogen estimation (Micro Kjeldahl) was 290 mg./100 ml. and electrophoresis showed a normal fibrinogen band.

Discussion

Many explanations of the disappearance of the circulating fibrinogen in this condition have been formulated and numerous cases described and investigated. The following points of agreement recur in the literature:

(1) The retroplacental haemorrhage precedes the fall in fibrinogen. The former, therefore, might be a precipitating cause, but is not an effect of the latter.

Dieckmann (1936) believed the bleeding tendency could not be the cause of the abruptio placentae as he had seen 4 cases of purpura haemorrhagica in pregnancy with no premature separation of the placenta. Reid, Weiner and Roby (1953) say that in their study of 1948, which included many cases with premature separation of the placenta, a number of fortuitous observations were obtained to indicate that failure of clotting power followed the placental detachment.

(2) In cases where the plasma fibrinogen is at a borderline level and a small inadequate clot forms, it usually rapidly disintegrates. This was at one time taken as clear evidence of the presence of a fibrinolysin, but it was found difficult in practice to demonstrate such a lysin when using an independent source of fibrin as a substrate. The interpretation of this phenomenon has, therefore, become doubtful.

Reid *et al.* (1953) say that this effect (dissolution of the clot), initially attributed entirely to the presence of a fibrinolysin, might be due to a fall in fibrinogen level to minimal levels for haemostasis, with or without the presence of a fibrinolysin. Jackson, Hartmann and Busby (1955) believe that with very low fibrinogen levels the clot is too weak to hold together the red cells.

(3) When the uterus is evacuated or removed, the fibrinogen rapidly and spontaneously returns to normal provided the patient has not, by this time, become too shocked.

Jackson *et al.* (1955) remark that their experience agrees with that of other workers—that once the uterus is evacuated the fibrinogen level will return to normal rather rapidly. It has been shown in general, they say, that serious bleeding will usually cease within 3 to 6 hours of evacuation of the uterus. This is our thesis, too.

(4) Fresh or stored blood transfusion will not alone, even on an heroic scale, restore the fibrinogen level while the patient remains undelivered.

Goodfriend, Shey and Siegelbaum (1953) explain this on the grounds that it is impossible to administer the whole blood at a sufficient rate to raise the patient's blood fibrinogen to effective coagulant levels. They maintain that each pint of blood with a normal fibrinogen level of 200 mg./100 ml. is so quickly diluted in the patient's circulation that its effect is minimal. This view appears to have had wide acceptance.

(5) Parenteral administration of prepared fibrinogen, or concentrated plasma, has been held to have a dramatic beneficial effect, even in doses which appear inadequate on grounds of simple arithmetic.

Jackson *et al.* (1955) mention a case in which the plasma fibrinogen level was zero when 2·38 grammes of fibrinogen were administered. At the end of 30 minutes the level had risen to 159 mg./100 ml. They comment, "once again we see a higher level of fibrinogen obtained than theoretically calculated". They conjecture that a small amount of fibrinogen must serve as a stimulus to further rapid production, or to release of further fibrinogen into the general circulation.

In the particular case they mention it does seem reasonably possible however to make the figures "add up". If we imagine the patient to have been a spare woman of 8 stone or 51 kg. she would in health have a plasma volume of about 5 per cent by weight of this, or 2½ litres, (Black, 1951). In a state of shock following haemorrhage one might imagine that the volume actually in circulation would be no more than 1½ litres. Then 2·38 g. of fibrinogen in 1½ litres gives a level of precisely 159 mg./100 ml.

In view of the general agreement that a fibrinogen level of between 60 and 100 mg./100 ml. is necessary for clotting efficiency (Biggs, 1955; Pinniger and Prunty, 1946; Alexander, De Vries and Goldstein, 1949; Stefanini and Petrillo, 1949) it is far more difficult to explain the favourable response to the very modest doses administered by Barnett and Cussen (1954). These were recorded as 404 mg. (Case 1) and 0·13 g. repeated twice (Case 2). One might have felt tempted to think that these patients had largely recovered spontaneously as ours did, but the detailed account of their Case 2 does not readily admit of this solution.

The Phenomenon of Incoagulable Blood

A marked fall in circulating fibrinogen, with or without incoagulability of the blood, occurs as a feature in a number of conditions. Explanations offered by various authors for the phenomena in abruptio placentae have been inspired by these conditions and may be classified thus:

Condition	Explanation
1. Simple blood loss with subsequent haemodilution playing a part.	GROUP A Simple physical loss and failure of synthesis.
2. After mobilization of fibrinogen at a particular site—as in the stage of pulmonary consolidation in lobar pneumonia.	
3. After experimental extirpation of the liver, or in hepatic failure due to chloroform poisoning, or in carcinomatous infiltration of the liver (Whipple and Hurwitz, 1911; Warren and Rhoads, 1939).	
4. After experimental injection of thromboplastin (Howell, 1941; Zucker, 1948; Schneider, 1950; Hartmann, Conley and Krevans, 1951).	GROUP B Thromboplastin theory.
5. After amniotic fluid embolus (Reid, Weiner and Roby, 1953).	
6. After retention *in utero* of a dead foetus.	
7. In the generalized Shwartzman or Sanarelli phenomenon (Sanarelli, 1924; Shwartzman, 1930; Gratia and Linz, 1932; Apitz, 1935; Thomas, 1952).	GROUP C Anaphylactoid theory.
8. In peptone and anaphylactic shock (Jacques and Waters, 1941; Nolf, 1905, 1908).	
9. After medical or surgical shock, etc. (Macfarlane, 1937).	GROUP D Fibrinogenolysin theory.
10. After sudden violent death (Morawitz, 1906; Macfarlane and Biggs, 1948).	
11. After surgical operations on the lungs (Soulier *et al.*, 1952).	

Group A

Based on the first group of cases Dieckmann (1936) made the suggestion that in abruptio placentae fibrinogen is initially lost to the circulation in the retroplacental haemorrhage. Secondly, further quantities might be taken from the circulating blood to form the retroplacental clot. Thirdly, as the liver is known to be the site of fibrinogen formation, and as the liver may be damaged in the toxaemias of pregnancy, liver failure could play its part in lowering fibrinogen.

But the liver does nothing to initiate the fall in fibrinogen, as numerous workers have recorded normal liver function tests and histology in these cases. Even more significant is that in abruptio placentae the fibrinogen falls first, while the prothrombin is affected later and to a lesser extent. On the other hand in experimental extirpation of the liver the prothrombin falls to low levels in a few hours, while the fibrinogen takes at least 24 hours to fall appreciably (Warren and Rhoads, 1939). It does seem possible that, once the fibrinogen level has fallen, whatever the cause, the intense generalized vascular spasm which occurs in these cases may involve the liver and prevent hepatic synthesis of fibrinogen for replenishment. Spasm, after all, is the probable cause of the all too common renal cortical necrosis (Sheehan and Moore, 1952). Thrombosis of the cortical vessels never occurs in the first 14 hours although it is found later.

Group B

A widely accepted proposition at the present time is that the defibrination in abruptio placentae is due to injection of thromboplastin into the maternal circulation. The thromboplastin is said to be derived from degenerate placental or decidual fragments entering the blood stream.

A great deal of experimental work supports this. The placenta has a high thromboplastin content. Using a single stage clotting assay, Schneider (1950) found 1,500 units of activity per gramme in decidua at term as compared with 200 units in lung, 50 in brain and kidney, 10 in liver and 1 in amniotic fluid.

Many observers have reported defibrination of the blood following the intravenous injection of thromboplastin or thrombin (Howell, 1941; Zucker, 1948; Hartmann *et al.*, 1951). When Schneider (1950) injected thromboplastin into mice the animals showed a prompt response by going into convulsions or coma. Within a few minutes they either died or recovered. Those that died had a characteristic lesion which was essentially a thrombo-embolism of the pulmonary arterial vasculature. Although this lesion was found in the animals which died, no such lesion was found in survivors. The effects described were taken to be the result of intravascular formation of fibrin. Animals which survived a just sub-lethal dose of thromboplastin sometimes developed complications from the resultant depletion of fibrinogen. As evidence that there was in fact a depletion of fibrinogen may be cited the experiences of Fulton and Page (1948). After a sub-lethal injection of fibrinogen there is a phase of resistance to further injection which lasts several hours. Animals in this stage of resistance are markedly deficient in fibrinogen, but sensitivity to further injections of thromboplastin can be restored by artificially replenishing the plasma fibrinogen.

However, as Schneider himself says, a straightforward finding in human post-mortem material comparable to the most readily obtained experimental lesions, namely a pulmonary thromboembolism, does not appear to have been reported.

Group C

Further objections to the Schneider hypothesis are made by McKay and his colleagues (1953). They concede that the mechanism may be at the root of some maternal deaths, for example those due to amniotic fluid embolism. But they maintain that, when the pathological findings in maternal autopsies in eclampsia, abruptio placentae, toxaemia, etc., are compared with those in Schneider's mice, one finds certain differences. Simply stated, the thrombi in human cases are for the most part on the side of the greater circulation rather than on the side of the lesser circulation. Hepatic, splenic, renal and pituitary arteries and arterioles of the gastrointestinal tract are found to be thrombosed. In

direct contrast, in animal experiments when thromboplastin is injected intravenously there are seldom any thrombi on the side of the greater circulation. From the histological standpoint a more close comparison can be made between the human autopsy material and changes seen in animals subjected to the generalized Shwartzman reaction. In this condition, if two intravenous injections of certain bacterial filtrates, spaced by about 20 hours, are made into rabbits, the animals die in a state of profound shock with haemorrhagic diathesis. If pregnant rabbits are used for the experiment (Apitz, 1935), or rabbits primed with a large dose of cortisone (Thomas, 1952), only a single injection of bacterial filtrate is necessary to produce the reaction. Gratia and Linz (1932) showed that the blood in these animals is incoagulable. They did not perform fibrinogen estimations. If blood is withdrawn from the affected animal and stood in a glass for 24 hours, it will not clot and the red cells will settle out. If now the supernatant plasma is subjected to a stream of CO_2 for 20 minutes they claim it will clot. Whatsoever may have been the cause of the incoagulability of the blood in these cases, therefore, it does not appear that it was due to lack of fibrinogen.

Although the Shwartzman or Sanarelli reactions are not identical with those of anaphylactic shock Gratia and Linz showed that survival from a generalized Shwartzman reaction protected the animal for some time against the assaulting dose of an anaphylactic reaction and concluded that the two phenomena must be closely related. Gratia and Linz are concerned to show that the generalized Shwartzman reaction is identical with the Sanarelli reaction described some years earlier.

Many authors have noted a marked increase in the clotting time in the blood of dogs in anaphylactic shock. Jaques and Waters (1941) investigated this problem. They utilized the neutralizing effect of protamine or heparin to titrate the level of heparin in the blood of dogs in a state of anaphylactic shock. They found it to be considerably raised. They also succeeded in isolating crystalline heparin from the blood of dogs in a state of anaphylactic shock, but were not able to do so from the blood of normal dogs.

Group D

In this group of cases where blood may become incoagulable the plasma fibrinogen is depressed or absent.

Morawitz (1906) studied the phenomenon of fluidity of the blood in cases of sudden or violent death. He found that the blood in such cases contained no fibrinogen itself and was capable of destroying the fibrinogen and fibrin of normal blood.

Judine (1936) has created keen interest. In Russia it was common practice to use the blood of corpses for blood transfusions and the most obviously suitable cases were victims of accident and sudden death. It was found that in these cases, after blood had been withdrawn from the body it clotted in the normal way, but became fluid again a few hours later and could then be used for transfusion without an anticoagulant.

Since it appeared that shock must be the relevant factor, Macfarlane (1937) investigated the occurrence of fibrinolysis in patients who had undergone surgical operations. There was an occasional lysis of whole, clotted blood, but this was a capricious occurrence. It was found that fibrin prepared from diluted plasma, however, disappeared in a high proportion of cases though similar preparations made before the operation were stable for weeks.

Macfarlane and Biggs (1948) conclude that there exists in normal blood a proteolytic enzyme, plasmin, its precursor plasminogen and its inhibitor antiplasmin. Plasmin activity can be produced *in vitro* by the action of streptokinase which activates plasminogen or by chloroform, which destroys antiplasmin. Enzymes resembling plasmin have been found in various tissues—particularly lung. Plasmin activity may occur in the living subject following various stimuli such as fear, trauma, severe exercise or the reaction produced by an injection of adrenalin.

Lewis and Ferguson (1952) have made studies on fibrinolysis in the dog. They believe the mechanism can be represented as follows:

Fibrinolysokinase←——Antifibrinolysokinase
(acting on)
Profibrinolysin——→Fibrinolysin←——Anti-
fibrinolysin.

Profibrinolysin may be taken as synonymous with plasminogen and fibrinolysin with plasmin.

The profibrinolysin in the serum of the dog may be activated to fibrinolysin by at least three fibrinolysokinases.

(*a*) Derived from many tissues. Lung tissue is a particularly powerful source.
(*b*) Derived from the plasma.
(*c*) A staphylokinase produced by certain staphylococci.

Soulier *et al.* (1952) report 8 cases of death in the course of operations on the lung in which the blood became incoagulable and fibrinogen could not be demonstrated in the plasma. They invoke the mechanism described by Lewis and Ferguson to explain the phenomenon. The inactive profibrinolysin, which is known to be present in the blood in sufficient quantity to destroy all the circulating fibrinogen and other proteins as well, under the action of a kinase of tissue origin, becomes active fibrinolysin. Under its influence not only may fibrin be dissolved but fibrinogen may also disappear from the circulating blood.

Writing in this same issue of the *Revue d'Hématologie*, Kaeser describes a case of premature detachment of the placenta with a fall in plasma fibrinogen and incoagulability of the blood. He observes that the cause for the fall in fibrinogen has not definitely been established but that there is reason to believe that placental products entering the maternal blood stream must play an important role. Some believe the significant substance to be thromboplastin and others that it is a fibrinolysin or fibrinolysokinase.

In the same volume again Baumann reports a case of lobectomy in which the blood became incoagulable. Fifty mg. of protamine sulphate were then injected intravenously and a quarter of an hour after this a further specimen of blood clotted in 5 minutes. This suggested that a rise in plasma heparin level played some part though there was no direct proof of this.

Conclusion

It seems likely that many factors may be involved in the phenomenon of hypofibrinogenaemia in abruptio placentae.

Summary

An account is given of the successful treatment of a case of abruptio placentae with afibrinogenaemia by immediate Caesarean section. Recovery of clotting power of the blood occurred soon after evacuation of the uterus without administration of concentrated fibrinogen and after only 1½ pints of stored blood had been given.

Some speculative remarks are made about various problems associated with the condition.

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PREGNANCY IN A BICORNUATE UTERUS COMPLICATED BY THE PRESENCE OF A TRANSVERSE VAGINAL SEPTUM

BY

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A TRANSVERSE vaginal septum is a rare cause of obstruction to the descent of the foetus through the birth canal. In 1939 Davids collected 23 cases from the literature and added 2 of his own. No further cases are described in the English literature until 1954 when Bowman and Scott recorded their case. Although few references are to be found the standard textbooks give one the impression that the problem is one which every obstetrician will meet at least once in a lifetime: Donald (1955) and Mayes (1955) each record a personal case.

CASE REPORT

A primigravida, age 24 years, was first seen at the antenatal clinic towards the end of September, 1953. She gave a history of the menarche at the age of 12 years and thereafter a menstrual cycle of 28 days. The menstrual flow lasted from 3 to 5 days and was of average amount and accompanied by lower abdominal discomfort on the first day. The L.M.P. was on the 23rd June, 1953. She was married in June, 1951 and had taken contraceptive precautions until the beginning of 1953. Coitus was painless. There were no previous illnesses of note in the medical history and the patient stated that as far as she knew she had not had inflammation or injury of the vagina in childhood. On physical examination it was found that she had a symptomless mitral stenosis. The uterus was palpable in the lower abdomen and corresponded with a period of amenorrhoea of 12 weeks.

Pregnancy progressed uneventfully and at the 34th week it was noted that the presentation was a breech. The uterus was asymmetrical and the greater portion of the body of the foetus lay to the right of the mid-line. Radiographic examination confirmed the presentation and demonstrated that the legs were extended. On vaginal examination the external genitalia were normal and hymeneal remnants were present. The vaginal canal appeared to be of normal transverse calibre but only 5 cm. in length. No opening could be seen or felt in the dome of this blind pouch but a cervix could be palpated beyond the septum on rectal examination. External cephalic version was not attempted in view of the probability of a double uterus. X-ray pelvimetry was performed and the adequacy of the pelvis confirmed. The spontaneous onset of labour was awaited.

Labour started at 6 a.m. on the 4th April, 1954 and progressed rapidly. At 2 p.m. the breech was still high in the pelvis but the diaphragm was now so soft and thin that the 3-finger breadth dilatation of the cervix could be easily assessed through it, the tactile sensation being similar to that of rectal examination. An opening in the septum was not yet visible or palpable. At 5.15 p.m. the membranes ruptured and with a speculum meconium tinged liquor could be seen streaming through a central aperture, a few mm. in diameter, in the vaginal "vault". With the rapid descent of the frank breech on to the septum and its subsequent stretching the central aperture became palpable and was readily dilated to admit 2-finger breadths. This manœuvre was practically bloodless. Only the anterior lip of the cervix could be felt. By 9.30 p.m. the anterior buttock was distending the perineum and an assisted breech delivery was carried out with minimal interference other than episiotomy and the application of Wrigley's forceps to the aftercoming head under Pentothal. Anaesthesia was continued with nitrous oxide, oxygen and trilene to allow manual exploration of the vagina and uterine cavity. The tags of mucosa forming the periphery of the septum were felt and the integrity of the vaginal walls confirmed. The congenital uterine abnormality was found to be a uterus bicornis unicollis with the placenta attached in the right horn. The left horn was a narrow canal. Manual removal of the placenta was carried out. The baby did not require resuscitation and weighed 7 pounds 3 ounces (3,130 g.).

The puerperium was uneventful. The remains of the septum were still palpable, mainly on the posterior vaginal wall, on the 9th day. A section of the membrane was taken for histological examination. It was composed of fibrous tissue with squamous epithelium on both surfaces. Intravenous pyelogram did not reveal any congenital abnormality of the urinary tracts. At the postnatal visit a narrow ring of fibrous tissue marked the site of the diaphragm at the junction of the middle and upper thirds of the vagina. This stricture just admitted 2-finger breadths. A hysterogram was performed and a

permanent radiographic record obtained of the uterine anomaly.

The patient attended the antenatal clinic again in January, 1955 with a history of 3 months amenorrhoea. Pelvic examination confirmed that she was again pregnant. The stricture was barely appreciable. Pregnancy progressed uneventfully and again the presentation was a breech and on this occasion the legs were flexed. Labour began spontaneously in the 40th week and after a first stage of approximately 20 hours successful assisted breech delivery was performed. The pregnancy was again present in the right horn. The baby weighed 8 pounds 7 ounces (3,700 g.).

Comment

The septum is of congenital origin: a diaphragm-like structure is not likely to be a sequel of vaginal inflammation or trauma. It is probably due to failure of canalization of the solid vaginal plate, a process usually completed by the 162 mm. stage of development (Hamilton, Boyd and Mossman, 1952). An alternative view is that the septum represents a lack of fusion of the Müllerian derivature of the vagina and the urogenital sinus. The presence of a double uterus in the upper genital tract makes this theory appealing when one postulates an abnormal propensity of the Müllerian ducts at different levels. To support it one should find columnar and not squamous epithelium on the upper surface of the membrane. And although the exact boundaries of the Müllerian and urogenital sinus derivatures of the vagina are still uncertain, Koff's view that the upper $\frac{4}{5}$ths is derived from the Müllerian ducts and the lower $\frac{1}{5}$th from the urogenital sinus, is generally accepted. The septum is thus lying at a higher level in the vagina than can be explained by a lack of union of these embryological structures.

The degree of occlusion of the vagina varies and ranges from the well developed transversely disposed diaphragm in which the opening can only be found after prolonged search under anaesthesia to mere strictures along the course of the vagina. With a severe degree, labour may be obstructed and severe bursting damage to the vagina caused, particularly if the diaphragm is thick with a broad firm base. This patient had a thin and membranous septum which became elastic during the last few weeks of pregnancy and stretched readily under the pressure of the oncoming foetal breech. It is probable that under pressure tearing would have occurred and the obstruction been overcome spontaneously. Digital dilatation of the aperture (chiefly tearing) was simply performed with good results. The remote result, as far as residual stricture formation is concerned, has also been excellent—neither dyspareunia between pregnancies nor difficulty with the second pregnancy being noted. If the malformation is severe assessment of the degree of obstruction should be postponed until late in pregnancy when the softening of the tissues is maximal and the distensibility of the vagina can be estimated with accuracy. If the obstacle to vaginal delivery is serious manual dilatation or incisions sufficiently extensive to allow descent of the foetus may so weaken the vaginal sheath that the bursting strain will produce longitudinal tearing and may involve the unprotected bladder and rectum. Caesarean section is preferable with dilatation of the aperture of the diaphragm following operation to allow drainage of the lochia. Stabler (1955), however, recommends that the diaphragm should be excised during pregnancy in all the severe degrees and with his technique to produce a battlement shaped scar a circular post-operative stricture can be avoided.

Summary

A case of obstructed labour due to a transverse vaginal septum is described. The origin and the treatment of the anomaly are discussed.

I wish to thank Dr. C. E. B. Rickards for permission to publish this case.

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A CASE OF ANEURYSM OF A UTERINE ARTERY

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ANEURYSM of the uterine artery or its branches is rare and a careful search of the literature has revealed only 17 cases. Of these, 12 (Berlin and Horwitz, 1952; Dubreuil and Loubat, 1926; Elkin and Banner, 1946; Gardner, 1954; Garnes and Greenwald, 1953; Graves and Smith, 1927; Kustner, 1917; Munde, 1898; Phelip, 1948; Raymond, 1908; Reynolds, Owen and Cantor, 1949; Williams, 1954) occurred in gynaecological practice, and in at least 7 a correct diagnosis was made prior to operation. In this group of 12 gynaecological cases there were no fatalities.

The remaining 5 cases (Hewitt, 1867; Kustner, 1890; Lowson, 1912; Mars, 1891; Vogelsanger, 1908) were obstetrical and were undiagnosed prior to autopsy. Four of these were reported in detail by Lowson (1912) who added a further case of his own. We have been unable to find record of any further cases and the following report is submitted not only on account of the rarity of the condition but, in addition, because it would seem to be the first case to be reported of a traumatic aneurysm following Caesarean section.

CASE REPORT

Mrs. J.H. was admitted to the Liverpool Maternity Hospital in labour on the 24th April, 1955. She was a primigravida, aged 40, who had been married for 11 years and had been investigated on two occasions for childlessness.

The first was in 1953 when tubal insufflation was found to be negative at a pressure of 220 mm. On the second occasion, in April, 1954, hysterosalpingography showed a normal uterine outline. The right tube had filled with contrast medium and a little peritoneal spill was demonstrated in the 24-hour film. There was no filling of the left tube.

Apart from an appendicectomy in 1934, no serious or relevant illnesses had occurred.

The date of the last menstrual period was 1st July, 1954 and the initial antenatal attendance was in the following September. Examination at that time showed no evidence of any general disease, and confirmed the presence of an intra-uterine pregnancy of 10-weeks duration. The pelvis was adequate, the blood group A Rh positive and the Kahn reaction negative. The blood pressure was 120/70 and there was no albuminuria.

There were no abnormal findings at any subsequent antenatal visit; the routine urine tests for albumen were consistently negative and the highest recorded blood pressure was 130/90.

Pains commenced at 6 p.m. on 23rd April, 1955, but the patient delayed her admission to hospital until 10.15 a.m. on the following day. The contractions had continued throughout the night and had apparently been strong and frequent. There was no history of rupture of the membranes.

Examination at the time of admission showed the temperature, pulse and respiration rates to be normal. The blood pressure was 170/100 and the urine contained a trace of acetone and a moderate amount of albumen. Abdominal examination showed the presenting head to be engaged in the pelvis in the right occipito-transverse position. The foetal heart was heard and was regular. On vaginal examination the cervix was 4-fingers dilated and thin with the head well applied. The lowest part of the head had reached the level of the ischial spines and the membranes were intact. Pethidine, 100 mg., was given, and repeated at 4-hourly intervals.

At 1.30 p.m. the pains of labour were suprapubic in site, and in character a constant dull ache with inter-

mittent exacerbations. On examination of the abdomen the uterine contractions were found to be irregular in frequency and duration. The colon was not distended nor was the bladder palpable. Rectal examination showed no change in the dilatation of the cervix. The blood pressure was 150/90.

The membranes ruptured spontaneously at 2 p.m. and it was noted that the liquor was meconium-stained. The foetal heart rate remained regular.

At 8 p.m. the patient expressed a desire to bear down, although rectal examination showed the cervix to be incompletely dilated. The labour of this elderly primigravida had now lasted for 26 hours and in view of this a vaginal examination was made to assess progress and to decide the mode of delivery. No change was apparent from the previous examination made shortly after admission.

On account of the lack of progress due to incoordinate uterine action, it was decided to perform a Caesarean section. An intravenous drip of 5 per cent glucose was commenced to combat the acetonuria.

At 9.15 p.m. the operation was commenced. Following a transverse incision into the lower uterine segment, the head was eased out with Wrigley's forceps. The delivery of the shoulders was difficult, and, in view of the disorderly uterine action in labour, it is possible that a contraction ring was present. Unfortunately, a hand was not passed into the uterine cavity to establish this.

As the infant was being delivered through the uterine incision, the mother was given 1 mg. ergometrine intravenously. Following delivery the placenta was removed by cord traction, examined and found to be complete.

The infant, a female child weighing 8 pounds, cried well at birth.

Green-Armytage forceps were applied to the upper and lower edges and to the two angles of the uterine incision, which was then closed in two layers. A continuous suture of No. 1 plain catgut was used for each layer. The blood loss during the course of the operation was not greater than normal.

The peritoneum covering the lower segment was closed. The abdominal wound was sutured in layers.

At the conclusion of the operation, when the patient was being transferred from the operating table to the trolley, a brisk vaginal loss of approximately 10 ounces occurred. The uterus was expressed of clots and 0·5 mg. of ergometrine was given intravenously. The patient's condition was satisfactory, the blood pressure being 130/80, and the pulse rate 100 beats per minute.

A further vaginal loss of 15 ounces took place at 11 p.m. and examination showed the uterus to be relaxed. The blood pressure was then 110/80 and the pulse rate 112 beats per minute. Morphia, gr. ¼, was given subcutaneously and Pitocin, 10 units, administered intramuscularly. Although there had been no further external bleeding and the uterus had remained well contracted, at 1.30 a.m. on the 25th April, 2½ hours after the conclusion of the operation, the systolic blood pressure had fallen to 80 mm. and the patient showed early features of shock. A blood transfusion was commenced and at 2 a.m. the blood pressure had risen to 110/80 and was subsequently maintained at this level. One pint of blood only was given.

The vaginal loss on the 1st post-operative day was greater than normal, but subsequently the puerperium was uneventful. No antibiotics were given, and, apart from a temperature of 99·4° on the evening of the 3rd puerperal day, the temperature chart was normal throughout.

The patient was discharged from hospital on 6th May, 1955, that is on the 12th day after operation. The infant had made good progress and weighed 8 pounds 7 ounces.

At 6.30 a.m. on the 10th May, 1955, 4 days after discharge from hospital (the 16th post-operative day) the patient had a sudden and profuse loss of blood vaginally. The obstetrical flying squad was called and on examination at 7.30 a.m. the patient was pale and shocked. The systolic blood pressure was 60 and the diastolic pressure could not be recorded. A transfusion of Group O Rh negative blood was commenced immediately and 30 mg. of methedrine and 0·5 mg. ergometrine were given intravenously.

At the start of the third bottle of blood, the patient was still bleeding vaginally, but there was great improvement in her general condition. The blood pressure had risen to 120/80 and it was considered safe to transfer her to hospital.

On arrival her general condition was moderately good, the blood pressure being 100/70 and the pulse rate 110, although the patient was still bleeding.

It seemed likely that the profuse bleeding was due to retained placental tissue, and, in view of this, it was decided to explore the uterine cavity. This was done under general anaesthesia using a pair of sponge forceps, and later a blunt curette. A large amount of clot was removed together with a few pieces of tissue which, on subsequent histological examination, were shown to consist of congested endometrium.

During the course of the operation the blood loss continued, and, as it persisted after exploration, the uterus was packed with gauze. There was no evidence of afibrinogenaemia and the shed blood clotted quickly.

Post-operatively the blood pressure was unrecordable, but some fifteen minutes later it had improved to 100/70. A total of 7 pints of blood had been given.

The uterine packing appeared entirely successful in that there was no evidence of bleeding either externally or internally. The general condition of the patient improved and the blood pressure rose to 130/75 and was subsequently maintained at this level.

On the 11th May at 9.30 a.m. the packs were removed. A profuse and uncontrollable haemorrhage occurred immediately, and in spite of the resuscitative measures of rapid intravenous and intra-arterial blood transfusion under pressure, the patient died at 10 a.m.

Post-mortem Examination

The autopsy was performed 4½ hours after death.

The body was that of an adult female of

normal build and showed a marked general pallor. The relevant pathological findings were confined to the uterus and are described in detail below.

The other findings were: a small acute abscess in the left breast; a haematoma 2×1×1 cm. in the subcutaneous tissues underlying the abdominal incision; pallor of the viscera and an involuting corpus luteum in the right ovary.

There were no signs of toxaemia, nor was there any evidence of sepsis.

Uterus

The uterus was approximately the size of a twelve-weeks gestation. An intramural fibroid 4–5 cm. in diameter was present in the left postero-lateral aspect of the body of the uterus.

The peritoneum of the lower segment at the site of the operative incision was puckered, and here and there a strand of catgut was present. Beneath the peritoneum of the right lateral half of this area was a small linear haematoma which was expanded a little at the extreme right.

The uterus was opened along the midline posteriorly.

The cavity of the uterus contained approximately 22 grammes of blood clot which was carefully removed. The placental site was identified on the posterior and right lateral walls of the uterine fundus and there was no evidence to suggest that it extended into the lower segment. A careful search for placental remnants was made but none were found.

On the endometrial surface of the lower uterine segment, in the line of the operative incision and towards the right of the midline, was a small dark swelling. The surface was not intact, and dark blood clot was visible in the depths of the swelling. The appearances suggested a haematoma or an aneurysm, probably the former. The remainder of the uterine incision was soundly healed.

The uterus was cleanly divided in such a manner as to bisect the "haematoma" (Fig. 1(*a*) and (*b*)). Inspection of the cut surface of the uterine wall showed that the "haematoma" corresponded in site with the subperitoneal haemorrhage previously mentioned, and both lay in the line of the operative incision. Moreover, the myometrium at this site was patchily infiltrated with blood.

A tortuous vessel was seen in the myometrium lying at one point in close contact with the deeper aspect of the "haematoma", and the possibility of a traumatic aneurysm was now considered. The main uterine arteries were normal in site and appearance and bore no direct relationship to the swelling.

Histology

Apart from the confirmation of the acute breast abscess, the only significant histological findings were those obtained from a block of tissue incorporating the uterine wall and the middle segment of the swelling. Several sections of this block were examined.

A direct communication was observed between the lumen of a small artery and the base of the swelling (Fig. 2). A diagnosis of rupture of a traumatic aneurysm was made.

The wall of the aneurysm was formed from compressed, almost laminated, connective tissue. Internal to this, and continuous with the internal elastic lamina of the artery, was a thin continuous layer of fibrinoid material. The lumen of the aneurysm was filled with laminated blood clot.

Lying in apposition with the wall of the artery and close to the site of its communication with the aneurysm was a foreign body which appeared to be suture material, probably catgut (Fig. 3).

The small vessel and aneurysm were surrounded by healthy reparative granulation tissue. There were focal areas of haemorrhage, round cell infiltration and numerous macrophages, many of which contained haemosiderin.

The incision into the lower uterine segment showed complete and normal healing.

There was no evidence of sepsis or of any specific disease.

Discussion

The case we have reported in detail above is essentially one of post-partum haemorrhage, both primary and secondary in type.

A review of the pathological findings suggests that during the closure of the uterine incision a small artery was damaged. The histological demonstration of a piece of catgut close to the

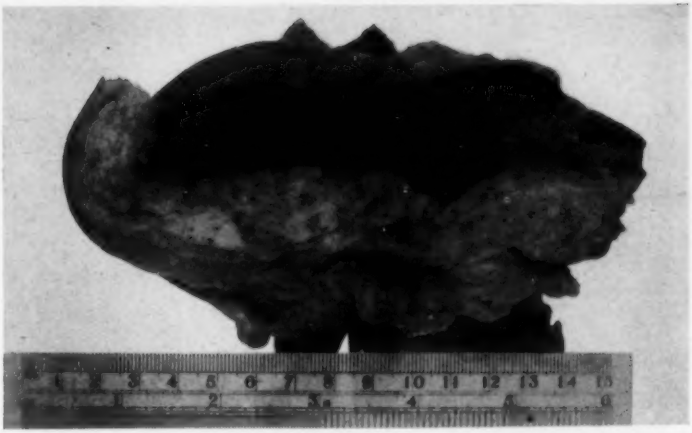

FIG. 1(*a*)
Longitudinal section through the uterus bisecting the aneurysm.

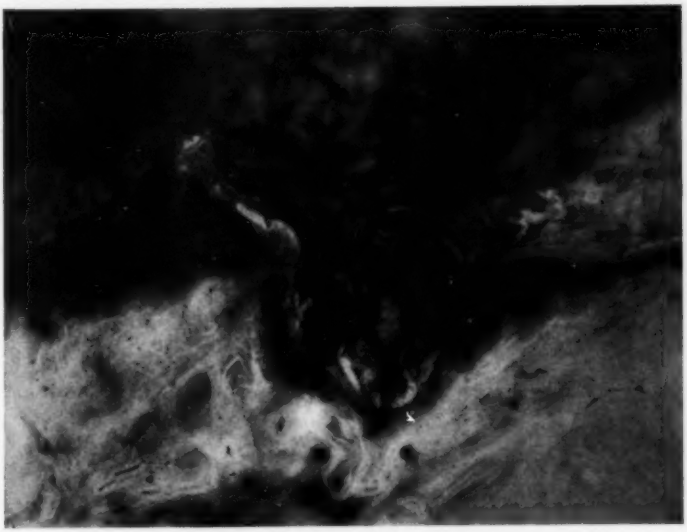

FIG. 1(*b*)
Photograph showing the aneurysm. ×2.

FIG. 2

Photomicrograph showing communication of the aneurysmal sac with the lumen of the vessel. ×7.

FIG. 3

Photomicrograph showing foreign body (catgut) at the side of the affected vessel. ×15.

M.H.M., K.B., J.B.L.

site of the aneurysm indicates that the trauma to the vessel was probably inflicted by a needle. Subsequently blood escaped from the damaged artery into the surrounding myometrium with the formation of a false aneurysm.

It is possible that a leakage of blood along the needle track accounted for the initial primary post-partum haemorrhage, but this can only be conjecture. On the other hand it is certain that rupture of the false aneurysm accounted for the secondary post-partum haemorrhage which ultimately proved fatal.

The lack of positive clinical signs by which the aneurysm could have been diagnosed is a disturbing feature of the case. Even more significant is the fact that a needle prick of a small branch of the uterine artery led to the formation of a false aneurysm which subsequently ruptured with fatal haemorrhage.

Had it been possible to diagnose, by some means or other, that the bleeding was in fact due to rupture of a false aneurysm, immediate hysterectomy would have been indicated. As it was there were no special features to distinguish the case from any other secondary post-partum haemorrhage.

Acknowledgments

We should like to thank Sir Arthur A. Gemmell and Professor H. L. Sheehan for their interest and helpful criticism.

We should also like to thank Mr. F. Beckwith, Chief Technician of the Department of Pathology, University of Liverpool, for the photographs.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

AT the Meeting of Council held in the College House on Saturday, 26th May, 1956 with the President, Mr. Charles D. Read, in the Chair, the following were elected to the Council to fill Statutory vacancies:

As representatives of the **Fellows:**

LONDON	Frank Cook.
ENGLAND AND WALES (excluding London)	Samuel Walter Maslen-Jones. John Arthur Stallworthy.
SCOTLAND	David McKay Hart.

As representatives of the **Members:**

ENGLAND AND WALES (excluding London)	Dorothy Margaret Shotton.
SCOTLAND	Matthew Garrey.

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Alexander David Telford Govan.
Sydney Wallace Jefcoate Harbutt.
Stanley Henderson.
Derek Jefferiss.
Norman Kenneth Bernard Kimbell.
Parvati Malkani.
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Mehroo Dinshah Aziz.
Peter Bryan Bailey.
Jean Lesley Baker.
Patricia Baker.
Jacqueline Elizabeth Banbury.
John George Banton.
Richard Campbell Begg.
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Geoffrey Berry.
John Raymond Birkett.
David Bartlett Bower.
Patricia Mary Boyd.
James Bradshaw.
Cynthia Adela Ruth Bray.
Roy Alexander Briggs.
Gordon Brill.
John Aloysius Browne.
Christopher John Buckingham.
Harry Mitchell Buckland.
Michael James Vendy Bull.
Robert Anthony Butler.
David Swainston Carroll.
Robert Chalmers.
Geoffrey Victor Price Chamberlain.
Elizabeth Pamela Cloake.
John Bartholomew Coldrey.
John Arthur Collings-Wells.
Diana Jean Collins.
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Anne Morris Cormack.
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George Roland Cubitt.
Maria Wiktoria Dabrowska.
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Alice Louisa Davis.
Leslie Roy Dennis.
Albert Edward Lewis de Thierry.
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THE NINTH ALL INDIA OBSTETRIC AND GYNAECOLOGICAL CONGRESS

THE Ninth All India Obstetric and Gynaecological Congress will be held in Amritsar on 29th, 30th and 31st December, 1956. The main subjects for discussion will be:

(i) Cardiac diseases complicating pregnancy.
(ii) Malignancies of the body of the uterus.
(iii) Statistical survey of (i) Eclampsia and (ii) Menarche and Menopause.

The Obstetric and Gynaecological Societies all over India, as well as the teaching institutions and practitioners in the profession, are invited to take part in the deliberations of the Conference.

Those desirous of reading papers on any of the above-mentioned main subjects or any other subjects are requested to communicate the title of their paper to us by the 1st September, 1956 and submit typed copy of the paper *in duplicate* with abstracts of the same also in duplicate by the 7th October, 1956.

Obstetric and Gynaecological Society of Northern India,
Benjamin Road, Ludhiana.

B. L. KAPUR, *Honorary Secretary*

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REPORTS OF SOCIETIES

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

Report of a Conference held at the Royal College of Obstetricians and Gynaecologists on 29th June, 1955 on

Cytology in the Diagnosis of Carcinoma of the Cervix

Chairman: Sir William Gilliatt (Chairman of the Scientific Advisory Committee of the R.C.O.G.).

The Chairman welcomed all present and thanked those who had sent in papers so that they could be circulated before the meeting. The Conference had been arranged so that those who are working in cytology should have an opportunity of discussing their methods and results, and of expressing the pros and cons of cytodiagnosis. He wished to express the gratitude of the Scientific Advisory Committee for the continued generosity of the British Empire Cancer Campaign in paying the expenses of this Conference.

Sir Arthur Gemmell (P.R.C.O.G.) expressed his pleasure that this scientific conference should be taking place in the College House. He welcomed all the members of the Conference and hoped that their discussion would have far-reaching and valuable consequences. The problem as he saw it was how to make the best use of this particular diagnostic method and to discuss the practicability of screening the female population generally and not only those attending gynaecological out-patient clinics.

The question of the best method of taking smears seemed to be a matter of preference, some liking the Papanicolaou pipette, and others the Ayre spatula, while many people advocated both methods. The gleanings from the Ayre spatula took less time to screen and might, therefore, miss more cancer of the body, while not missing cancer of the cervix. Should they have teams in which fully-trained technicians in cytology did the screening, or should the matter stay in the hands of individual cytologists? What should be the field in home-screening, and on what scale should it be attempted?

Dr. A. F. Anderson (University of Edinburgh). The results obtained after nearly 6 years work (up to the end of May, 1955) were summarized. The material was mainly derived from the gynaecological out-patient departments of four Edinburgh General Hospitals (two of which were teaching hospitals). There were 9,910 cases from these hospitals. A contraceptive clinic had yielded 2,834 cases, but this had proved an unfruitful source, as the incidence of carcinoma had dwindled from 7 cases in the first 1,000 cases to 1 case in the second 1,000, and none in the next 800 cases. A new source in the patients of general practitioners had been more rewarding, and 176 cases had recently been studied. The total of 12,920 patients screened did not include women with clinically obvious cancer.

Ayre's technique was usually employed; aspiration smears were only used in special circumstances. Two women technicians (Miss MacBryde and Miss Cockburn, the latter only part-time) had been trained to take the smears from the patients. The technicians screened all the smears, and passed any doubtful and "suspect" smears to Dr. Anderson. They did not apportion their time in any particular way as they had other work to do, but they had found that they could deal with 15 to 20 smears daily.

Cervical cancer. Dr. Anderson thought that "percentage accuracy" was a misleading way of assessing the value of cytology, and preferred to report the results as shown by the discoveries of clinically unsuspected cases, of which there were records of 108:

		Cases
9,910	patients from gynaecological clinics yielded	98
2,834	patients from a contraceptive clinic yielded	8
176	patients from general practitioners yielded	2
12,920		108

Of these cases 37 were invasive (34 per cent) and 71 were intra-epithelial. The following cases were not treated by radiotherapy or radical surgery, but as below:

Amputation of cervix only	16 cases
Biopsy and cauterization only	12 cases
Cauterization without biopsy	5 cases

In 9 cases that were watched by smears without biopsy for periods varying from 12 to 33 months, all were eventually confirmed by biopsy.

The false positive and negative results were:

	First 1,000 Cases	Cases 1,001-3,000	Cases 3,001-4,680	1953	1954	1955
False positive	11	1	1	1	1	0
False negative	4	2	1	2	2	3

Dr. Anderson went on to comment: Professor McKelvey has said of the study of carcinoma-in-situ that it should be carried out in special study groups where meticulous men carefully and critically evaluate their decisions—"This is a game in which the rules should exclude those who cannot or will not make their own histological evaluations. Otherwise it becomes a dreadfully dangerous pastime. It is essential that the player be a chronic

worrier and that he become so suspicious of even his own carefully drawn conclusions as to believe that almost nothing is final." We believe that these remarks apply with equal force to cytology, but, although we like to think that we have built up such a study group in Edinburgh, it does not always include the clinician, and we constantly emphasize that the responsibility is the clinician's and that ours is merely a step in the diagnosis. Some clinicians accept the method as an established helpful step in diagnosis and discussion with them is easy; others need much more careful handling lest they be frightened off by a false negative or positive report, or their interest be not sufficiently stimulated to follow a case properly.

Information about each case is essential if reports of any significance are to be offered, and smears cannot be pronounced upon like blood cell counts. If there is clinical suspicion but a negative smear, we have always advised that the smear report should be ignored. On the other hand some positive smears must still be regarded as positive if a negative report is obtained from inadequate biopsy material.

Some clinicians are reluctant to believe that there may be a cancer which they cannot see, and biopsies tend to be inadequate in such cases, if they are done at all. In the absence of a clinical lesion the biopsy must be bigger, not smaller.

It has sometimes been regretted by those practising smear interpretation that a great many negative reports are not confirmed by biopsies, but I would submit that a single biopsy is quite inadequate to contradict a *positive* smear, let alone confirm a *negative*, if the cervix looks benign; and that, if it looks benign and the smear is negative, an *adequate* biopsy is unjustifiable without very suggestive symptoms. We make 10 to 20 blocks from every removed cervix sent to our laboratory, unless there is an obvious cancer, and we can see no point in the cervix being sent to us if we do not subject it to this degree of scrutiny.

To complete these observations on what is entailed by the phrase "a study group" I would like to explain that all our intra-epithelial cancers treated by total hysterectomy have had the remainder of the cervix examined in 10 to 20 blocks, and also 6 from the cut edge of the vaginal cuff (after Meigs and Graham). Ring biopsies, coning biopsies, and amputated cervices are similarly divided during the diagnostic period, and serial sections often have to be carried out to demonstrate very small cancers. This complies with McKelvey's "worrying", but a positive smear justifies all this attention.

The percentage accuracy of diagnosis of non-clinical cancer. The percentage accuracy myth has been exposed long ago, and the figures can of course be weighted if obvious clinical growths are included, even if these occasionally have a negative smear. Even in series of cases excluding these, we do not believe it is a significant way of assessing the value of the method because of the large element of subjective impression in the clinician's opinion. Howard Taylor, junr., has pointed out that "one may at once dismiss the general figure for accuracy, which is about 98 per cent, as meaningless, for with less than 2 per cent of positives to be expected, a percentage success of 98 per cent should be obtained simply by guessing each slide to be negative".

It is sometimes very difficult to ascertain whether the clinician was or was not suspicious. We have omitted from our discoveries 2 cases in which positive smears were confirmed but in which two senior gynaecologists have disagreed about clinical suspicion. On the other hand we have credited our figures with a case whose cervix was described "looks innocent but should have biopsy". In such situations who shall decide if there is suspicion and who the value of the smear? Our figures are as honest a reflection of our value to the clinician as we can make them, but it is the clinician who will decide the value of the method to him and to his patients.

The watching of cases without treatment. The smear method may uncover exceedingly tiny growths sometimes requiring hundreds of sections to demonstrate them histologically. The biopsy, and the cauterization which usually follows it, may therefore easily act as treatment. Therefore the only cases "watched without treatment" are those not proven by biopsy, and many would regard these as unacceptable. We offer the cases quoted as our nearest attempt at this heading.

Corporeal cancer. We chose to use the Ayre spatula from the beginning, as we were concentrating on the commoner cancer, that of the cervix. It is probable that the aspiration vaginal smear (or an intra-uterine smear) is more likely to reveal cancer of the body, and it is when the problem included that possibility that we have sometimes requested an aspiration smear. Our interpretation of these cases has improved, but it is a rarer cancer, and it occurs at a later age so that patients usually seek aid sooner, and we are not surprised to find little benefit when we are correct, and no harm when we are wrong, provided that the ordinary routine investigations are carried out. (Dr. Anderson described a few cases to illustrate these points.)

DR. J. BAMFORTH (St. Thomas's Hospital, London). The cytological examination of vaginal smears in the diagnosis of malignancy has not been employed systematically nor on an extensive scale at St. Thomas's Hospital. Rather has a selection been made of interesting cases which presented unusual features of difficulty in diagnosis. Slightly over 1,000 specimens have been examined. These were chiefly obtained from the outpatient department, but a few came from the gynaecological wards. In each case two films were made, one obtained by a pipette or large platinum loop from the posterior fornix, and one from the squamo-columnar junction of the cervix by means of Ayre's spatula. All were stained by Dudgeon's technique. The smears were examined by one of two or, in some instances by two, pathologists. Eight cases of quite unsuspected carcinoma of the cervix have been found, and 4 of these were of the intra-epithelial non-invasive type. In every one of these 4 cases the gynaecologist had no indication where to take a biopsy, and after either conectomy of the cervix or hysterectomy radial sections were prepared and the diagnosis of malignancy was confirmed by histological

examination. In a very small number of cases histological examination failed to reveal any malignant focus when suspicious cells had been found. Almost every case of definitely invasive carcinoma of the cervix showed positive smears, but in carcinoma of the body 1 or 2 cases were missed and difficulty in distinguishing this condition from endometrial hyperplasia has been experienced.

Carcinoma-in-situ of the cervix uteri is not an isolated condition. Such lesions may occur elsewhere in the body, e.g., in the skin (Bowen's disease), anal canal, oesophagus, nose, and bronchial tubes. In the case of the cervix, biopsy and the method of serial section may be used to determine whether the small early lesion is invasive or non-invasive. In either case cytological examination shows that there are certain changes in the appearances of the cells themselves, that suggest malignancy. It is important to diagnose the condition in the non-invasive stage. It has been found that some cases regress, but that others may progress to frank invasive carcinoma. This change may take place after a variable interval of time. According to Ayre an average period of 8 years is required for a non-invasive carcinoma to become invasive.

PROFESSOR H. C. MCLAREN (University of Birmingham). An experiment has been in progress with a team including Professor H. C. McLaren, Mr. M. J. D. Noble, Mr. R. B. Parker and Dr. C. W. Taylor, to attempt to assay the reliability of the cytological method of diagnosis and to outline its place in gynaecological practice. There were two sources of material, a group of unselected out-patients (for the screening experiment) and a group of women with post-menopausal bleeding. The technique used was that of vaginal aspiration, carried out by the cytological technicians. From the start the diagnosis of abnormal cells was placed entirely in the hands of Miss M. E. Attwood, a senior technician who was sent to America for six months training. Miss Attwood has subsequently been training other technicians, but these are not solely engaged on cytology but have other laboratory duties.

Miss Attwood reported that the time taken for the examination of each smear in this first series represented about one hour's work, but most of this time was spent on training and checking trainees, on taking and staining the smears, and on the indexing of reports. The actual screening of the slide took the shortest time of all. The average time taken by a trainee to screen a slide is about 20 minutes but this falls to 7 minutes with experience. Every field is carefully studied and consideration must be given to ocular fatigue; four hours a day at the microscope is the maximum for efficient reading.

Professor McLaren summarized the results of screening consecutive gynaecological out-patients. A total of over 5,000 smears have now been taken, but, in this first series of 2,290 patients, smears were taken from 2,196; 40 children and 54 "lost" notes make up the total. Among these were a total of 33 cases of carcinoma of the portio or endocervix, 15 of corporeal carcinoma, 2 of corporeal sarcomata, with 32 cases of vulval, ovarian or recurrent carcinoma. All but one of the cases of cervical cancer were recognized by cytology, the single exception being an error, i.e., on review the smear was clearly positive. Of 15 cases of corporeal carcinoma and 2 of corporeal sarcoma the smear was positive in only 12. Unsuspected invasive carcinoma of the cervix was "picked up" by cytology only once. On the other hand, cytology led to a diagnosis of unsuspected carcinoma-in-situ in 5 cases and atypical epithelial hyperplasia (equivocal pathology) in 4. Carcinoma of the corpus was diagnosed as a result of a positive smear in a single case, i.e., in the presence of repeatedly negative clinical findings.

In a separate investigation 181 patients with post-menopausal bleeding were studied. Of these 31 were found to have adenocarcinoma, and 27 of these were recognized by the smear technique.

Professor McLaren went on to comment: if cytology discovered that 1 in 10,000 out-patients had carcinoma or carcinoma-in-situ the vast amount of work involved in the diagnosis would scarcely be justified. On the other hand, if the "pick-up" rate were 2 or 3 per cent, cytology would obviously have a definite place in any gynaecological out-patient service. The first task of the experiment, therefore, was to define exactly what is meant by a "pick-up" or surprise positive smear. It was found that the ordinary out-patient notes were inadequate; for example by no means every case in our out-patients had had a speculum passed. Accordingly a special case-sheet was evolved which required a detailed history and note of the findings including a rough drawing of the cervix. The case-sheet required the clinician to state whether he thought the patient had a carcinoma of corpus or cervix. On this basis a surprise positive smear could be measured against a careful negative clinical examination. We feel that it is important to record every "pick-up" in detail, and this will be done in our published report.

It was emphasized in the discussion that a positive smear is by no means a diagnosis. The whole clinical team is alerted by the smear to study all the facts, and to agree on further plans for ring biopsy, further smears, etc.

We feel that although it is a laborious technique there is a definite place for cytology when it is integrated into the work of a clinical team. The main use of the technique is to pick up the very occasional unsuspected case of invasive cancer. Carcinoma-in-situ can also be "spotted" by the technique, but whether or not it is ever justifiable to watch such a case without treatment will be hotly debated. The study of the natural history of carcinoma-in-situ must be carried out by a research team if useful information is to be obtained. For this reason the establishment of a cytological diagnostic centre without close liaison with an experienced gynaecologist and pathologist makes little appeal to the Birmingham group.

G. R. OSBORN (Derbyshire Royal Infirmary). Most of the smears examined were from women attending the in- or out-patient department of gynaecology. They were taken whenever the gynaecologist considered them indicated, not as a routine. The continuing request for approximately 1,500 examinations each year suggests

that cytology has a useful place in routine hospital work. Comparable satisfaction has not been obtained from the examination of smears taken from normal women in "cancer prevention clinics". The most interesting observation from these "well woman clinics" was that a number complained of developing a vaginal discharge after the first visit—fortunately in each case the smear taken on the first occasion showed the presence of trichomonads.

The aspiration (Papanicolaou) method of making the smears is preferred because it is easier to make perfect smears this way. Because of dryness some smears can only be made by swab. The use of the Ayre scrape method has been discouraged, the results frequently being neither cytology nor histology. Because of the undoubted existence of 5–10 per cent of false negatives with good technique the gynaecologist does sometimes require an additional method of the scrape type. Really excellent results are obtained by histological processing of superficial cervical curettings removed by a Volkmann spoon (method of Mr. N. L. Edwards); these are used in preference to cytological scrape techniques.

At least 50 per cent more infections with trichomonads are proved by cytological techniques than by wet smear. This is important for cross infections with this parasite are possible in the out-patient department and in the radiotherapy wards. The age incidence of this disease is quite different in venereal and gynaecological practice, the young women know it is a venereal infection and so attend that department—as do some in later age groups. Results for 1952 and 1953 are:

Age	V.D. Department (Mr. H. R. M. Richards)		Gynaecological Department	
	Cases	Per-centage	Cases	Per-centage
Under 20	36	41·4	3	1·3
20–29 ..	35	40·2	31	13·9
30–39 ..	11	12·7	54	24·2
40–49 ..	3	3·4	81	36·3
50–59 ..	2	2·3	41	18·4
60–69 ..	0	0·0	11	5·0
Over 70 ..	0	0·0	2	0·9

Personnel required. Dr. Osborn reported on all the smears himself. This is only a very small proportion of the work done in an unusually busy general laboratory. Only one technician (Miss J. M. Adamson) stained the smears; this again was a small part of the work she does. Research would be much easier with a more elaborate department; we consider we have proved that the work can be undertaken routinely in any good hospital laboratory. More time is taken on the clerical than the technical side. A pathologist rarely needs to spend more than 5 minutes on any smear, less experienced technicians do take appreciably longer—Miss Adamson's average time proves to be 14 minutes.

Percentage accuracy in cases of non-clinical carcinoma: This can only be answered by the gynaecologists. My experience, as a pathologist, is that the accuracy of the smear diagnosis does not depend on whether the cancer is obvious clinically or not. There are many cases where the initial diagnosis was entirely by cytology. Unfortunately there are some with negative smears in whom the cancer could be seen quite easily. The conclusion is that cancer can be overlooked on inspection, by biopsy and by cytology, but very few cases will be missed if all these methods are used. To determine the accuracy of the method it was thought better to consider the follow-up of all cytology reports, and the use made of cytology in every case of cancer of the cervix and body of the uterus.

Follow-up of cytology: Miss Adamson went through every report made in 1953 and 1954 and made a list of all cases reported as cancer, probably cancer or possibly cancer. The object was the check on "false negatives".

1953: 49 positive smears from 37 different patients reported thus:

29 cancer cells present—all proved correct,
12 cancer cells probably present—9 proved correct,
8 cancer cells possibly present—all were cases of cancer.

1954: 56 positive smears from 41 different patients reported thus:

32 cancer cells present—all proved correct,
18 cancer cells probably present—all proved correct,
6 cancer cells possibly present—3 proved to be cancer.

Of the 6 cases not proved 2 have been lost to follow-up and their condition is unknown; one proved to be cancer at laparotomy but the primary lesion is not proved; 2 had urethral caruncles; the lesion of the remaining 1 is unknown.

Review of all cases of cancer of the uterus 1950–1954 inclusive: 311 cases have been divided into 4 groups according to diagnostic methods.

A(1). Thirty-eight cases had preliminary investigation by cytology only. Results were: cancer cells present, 17 cases; cancer cells probably present, 8 cases; cancer cells possibly present, 3 cases; no tumour cells seen, 10 cases. Of the 10 "false negatives" 3 smears are too scanty for diagnosis, 6 are clearly negative and 1 might have had a doubtful report.

A(2). One hundred and forty-one had both biopsy and cytology before treatment. Cytological reports were: cancer cells present, 65 cases; cancer cells probably present, 29 cases; cancer cells possibly present, 17 cases; no tumour cells seen, 30 cases. Of the 30 "false negatives" 10 smears are too scanty for diagnosis, 12 are clearly negative, 7 might have had a doubtful diagnosis, 1 contains many cancer cells but they are so well differentiated that their nature was not determined; another smear was requested but not supplied.

B. Seventy-eight cases had preliminary biopsy but no cytology.

C. Fifty-two cases were diagnosed from the operation specimen with no preliminary biopsy or cytology.

In groups B and C the diagnosis was so obvious to the gynaecologist, as a rule, that cytology was not bothered with. This is unfortunate because it halves the number of positive smears seen by the pathologist and hampers research work. In future it is to be hoped that gynaecologists will take smears from these patients. Even if they do not need the result the cytology department needs the experience to apply with greater certainty when the diagnosis is not obvious.

D. In 16 of the above cases recurrence after treatment was first diagnosed cytologically. These are additional to the positives reported above and are grouped as follows: A(1) no case, A(2) 5 cases, B 8 cases, C 3 cases.

Of the 179 cases with pre-treatment cytology 14 had 2 or more smears. These multiple smears mostly agreed; in one the first smear was doubtful and the second definitely positive, in another both were negative.

The belief that the persistence of a high-oestrone type of smear after the menopause means that cancer is more likely to develop must be accepted with some caution. In 5 of the 40 "false negatives" the smear was of oestrone deficiency.

Comparison of Results in Cancer of the Body and of the Cervix

	Cervix	Body
Group A(1) (preliminary cytology only):		
Cancer cells present	16	1
Cancer cells probably present	8	0
Cancer cells possibly present	1	2
No tumour cells seen	8	2
	33	5
Group A(2) (preliminary cytology and biopsy):		
Cancer cells present	44	21
Cancer cells probably present	19	10
Cancer cells possibly present	5	12
No tumour cells seen	15	15
	83	58

The 132 cases without pre-treatment cytology are composed of 66 cancers of the cervix and 66 cancers of the body. The 16 recurrences diagnosed cytologically are from the cervix 10, and body 6.

Intra-epithelial carcinomata were found in 35, or 10·1 per cent of 346 cases. Many of the invasive cancers of the cervix gave histological evidence of arising from intra-epithelial lesions. The histologically doubtful group (basal hyperplasia progressing to carcinoma-in-situ) all gave negative cytology. Smears were positive in 21 and negative in 6 cases. Four of the women were aged 28. Four cases are under observation without active treatment. It appears probable that this will be a commoner practice in the future. Two types of case are suitable for observation: a young woman who wishes to have children, and an older woman who is not fit for operation. Before treatment is given in any case repeatedly positive cytology and a definite biopsy are usually required. One woman aged 28 became pregnant while this series was being examined. She urged the gynaecologist to perform a hysterectomy; no invasive neoplasm was found in the uterus but there was residual carcinoma-in-situ. Hysterectomy is probably not essential in these cases; although pregnancy increases the malignancy of most cancers it does not appear to accelerate the transition from intra-epithelial to invasive squamous cell carcinoma. Our experience is that, although intra-epithelial carcinoma may be an exceedingly small lesion, it is more often an extensive one—in an extreme case it was found to extend from the line of division of the vagina to the fundus of the uterus.

Conclusions. Cytology has a valuable part to play in routine hospital practice. Its cost is a mere fraction of that of the general pathology service of the hospital. The work is not tedious as it may be concerned with many conditions other than cancer. Cytology should be dominated by histology. It may lead to the cutting of some additional sections, but this work is not a burden if requests are made with discretion.

With perfect smears the false negative rate is about 10 per cent, but because some smears are unsatisfactory the total false negative rate is about 20 per cent. Fortunately the cases unrecognized by cytology are usually diagnosed by other methods. On the other hand cytology has sometimes made the diagnosis of cancer when other methods have failed.

The false positive rate should not exceed 3 per cent. An occasional false positive report is of no consequence in hospital practice, as action will not be taken upon it without other evidence, but unfortunate psychological disturbances have been seen after false positive reports in the "cancer prevention clinics".

Cytological and histological methods for the determination of radiation response do not appear to have been useful or reliable in practice.

Dr. Agnes L. Scott (Dumfries and Galloway Area, Scotland). In 1953 a routine cytological survey was started on patients attending the Central Gynaecological Clinic at the Royal Infirmary, Dumfries and at three peripheral clinics in the Area. The Area serves a population of 146,000. In all, 1,935 unselected and consecutive out-patients attending any one of these clinics have been investigated. The first 1,000 patients examined were between the ages of 20 and 45, and the remainder of the smears were taken from patients of all ages, except for a few of the younger patients when it was technically impossible to obtain a smear.

Smears were taken with Ayre's spatula and fixed immediately in ether-alcohol. They were then stained by Papanicolaou's method. Other stains used for experimental and comparative purposes were Gram's, Best's carmine, haematoxylin and eosin, P.A.S., and alkaline phosphatase. Each stained smear was examined by Dr.

Scott, the staining having been carried out by a technician. In order that the technician concerned might gain experience in the preliminary screening of slides she inspected all smears before they were referred to Dr. Scott; it is intended in due course, when it is evident that the technician is competent, that she shall carry out a preliminary survey of all smears. Under existing conditions, and with the present turnover of cases, the technician can prepare the smears in about two hours per week. Ten to fifteen smears can be scrutinized per hour on the average.

Among the 1,935 cases unsuspected carcinoma was discovered in 17 cases (12 stage O, and 5 stage I). Routine follow-up of cases of known carcinoma after treatment revealed 1 unsuspected vaginal recurrence 2 years after a Wertheim operation. In addition 1 case of carcinoma of the body of the uterus was discovered by cervical smears in the absence of clinical suspicion and prior to diagnostic curettage.

In every case in which a positive smear was obtained this was followed up by one or more ring biopsies of the cervix. All cases in which the biopsy confirmed the diagnosis of carcinoma were treated surgically, the nature and extent of the operation depending on the histology found and the age of the patient. Carcinoma-in-situ in a patient of the younger age group, with no histological evidence of invasion, was dealt with by total hysterectomy and on a few occasions by amputation of the cervix. In all other cases, i.e., those in which histological invasion was evident, Wertheim's hysterectomy was carried out. In several instances this operation appeared to be unduly radical, but previous experience had shown the unpredictable behaviour of even the earliest carcinoma. The radical operation was felt to be justified in the older patients, especially when they were parous.

In cases in which a positive smear was followed by a negative ring biopsy no operation was performed but these patients were kept under review with repeated smears and ring biopsies at 3- to 6-monthly intervals, depending on the particular histological picture found. At present 12 such patients are under review.

It is of interest that in a few cases in which the uterus was removed detailed examination showed that the original lesion had apparently been removed completely by the ring biopsy. On the other hand, a larger number showed, despite a very early histological lesion at the time of the biopsy, actual invasion in the post-hysterectomy specimen. This observation strengthens our opinion that radical surgery is required if the safety of the patient is to be assured. Nevertheless, there is the natural and human tendency to limit the extent of operation in the younger and nulliparous patients, and a review of the literature shows that a similar outlook generally obtains.

DR. A. I. SPRIGGS (Oxford). As far as possible smears were taken from all gynaecological out-patients, except those with clinically obvious cancer. The examining gynaecologist made one smear for each case, by the Ayre method. All smears were stained and screened by Mr. M. M. Boddington, and areas marked as abnormal were re-examined by Dr. Spriggs. Reports were at first sent out independently, but are now sent from the Department of Pathology. As Mr. Boddington has been examining sputa, serous fluids, etc., in addition to cervical smears, it is not possible to estimate the time spent on gynaecological work independently. The actual time spent in examination of a slide averages about 5 minutes.

The results obtained in the examination of 2,180 smears from 2,000 cases are shown in Table I.

TABLE I

	Smear Negative	Smear Positive
Proved invasive carcinoma	Body 5 Cervix 4	Body 6 Cervix 21
Carcinoma-in-situ and "epithelial instability"	0	Body 1 Cervix 13
Clinically and/or histologically negative ..	1,916	Body 7 Cervix 3
Follow-up not yet complete		11

In addition to the cases recorded in Table I there were 5 cases with abnormal cells in which a request for the smear to be repeated resulted in a second negative report, and 9 cases of cancer in which the smear was reported to be unsatisfactory and no second smear was provided.

Table II shows the proportion of lesions detected by the smear from cases in which there was clinical suspicion of carcinoma. The only criterion of this has been the reply of the gynaecologist to the question on the request form "Is there any clinical suspicion of carcinoma? If in doubt, answer Yes."

TABLE II

	Invasive Carcinoma of Cervix	Invasive Carcinoma of Body	Carcinoma-in-situ and "Epithelial Instability" of Cervix	"Epithelial Instability" of Endometrium
Carcinoma clinically suspected	18	6	1	0
Carcinoma clinically unsuspected	3	0	12	1

Several cases of intra-epithelial carcinoma or related lesions are being watched without hysterectomy or radiotherapy. The treatment of these has been: amputation of cervix 3, no surgery 6, lost to follow-up 1.

These figures confirm the results which have been obtained by others on much larger series both here and

abroad. *Unsuspected* early invasive cancer was found in 3 cases out of 2,000 screened (0·15 per cent), and carcinoma-in-situ and doubtful lesions of the kind were found in 13 (0·65 per cent).

With regard to large screening projects, attention is drawn to the conclusions of Shields Warren and his collaborators (Lombard *et al.*, 1952). After a 7-year study on behalf of the Massachusetts Department of Public Health they concluded that the cost per case of cancer discovered by the smear in women without symptoms was $1700, and that "it seems impracticable to consider the use of the vaginal smear as a routine screening procedure". This view must carry considerable weight, coming as it does from some of the earliest pioneers of the method.

It is probable that the results published in the literature are better than those which would be obtained if the cytological techniques were widely used. At present the work is mostly done by enthusiasts, but if it was done by persons with no interest in it, especially if they were insufficiently trained, the results would probably be poor. The cytological method is capable of saving lives, and is also an indispensable tool in the study of pre-invasive carcinoma, but it is an expensive refinement whose use should probably not be extended outside the larger centres.

Reference

Lombard, H. L., Middleton, M., Warren, S., and Gates, O. (1952): *New Engl. J. Med.*, **246**, 523.

Dr. Erica Wachtel (Hammersmith Hospital, London). In the past 5 years vaginal smears have been taken as a routine from every patient over 30 years of age seen in the wards or out-patient department of Hammersmith Hospital. The total number of smears taken during this time was 6,966. The aspiration method was preferred as it collects cells from the entire genital tract, whereas cervical scrapings only provide cells from the cervix. The slides were stained by a technician, but all the screening and reporting was done by Dr. Wachtel.

During the 5 years 133 carcinomata were diagnosed cytologically and histologically, including 70 squamous-celled cervical cancers, 4 squamous-celled vaginal cancers, a hidradenoma of the vulva, a squamous cancer of the clitoris, and 57 columnar-celled growths of the endocervix or body of the uterus.

Of the 70 squamous carcinomata of the cervix 63 were diagnosed correctly by the vaginal smear, one had an unsuitable smear, and 6 were not diagnosed. This gives a positive accuracy of 90 per cent. Nine of these squamous cancers were "in situ" lesions, and 6 of these were detected by the smear, but in 3 cases there were negative cytological findings on repeated occasions.

Four cases of early detection of carcinoma of the cervix were reported, and 3 examples of the early detection of recurrences after treatment of cervical carcinoma by operation or radiation. Only 1 case of carcinoma-in-situ with histological confirmation is being watched without active treatment being given. The lesion was diagnosed cytologically and histologically in March, 1954, when the patient was under treatment for an unrelated tubo-ovarian mass. She has since had many smears and biopsies, none of which have shown any abnormality, and it is concluded that the lesion was completely removed by the biopsy, or that it has since retrogressed.

In the 4 cases of carcinoma of the vagina the smear was positive, but not in the case of hidradenoma. The case of carcinoma of the clitoris was of particular interest. The patient was aged 57 and attended in the surgical department with an enlarged inguinal gland, which proved on section to contain secondary deposits of carcinoma. After an unsuccessful search for the primary lesion smears were taken from the clitoris, vulva, vagina, and cervix, and only that from the clitoris showed carcinoma cells. Biopsy confirmed this finding, but classified the lesion as carcinoma-in-situ. No evidence of malignant disease elsewhere was found. After radical vulvectomy no lesion was found in the specimen removed.

Of the 57 cases of columnar-celled carcinoma 50 (88 per cent) were diagnosed correctly by the smear technique. There were 3 unsuitable smears, and 4 cases were not diagnosed by this method. A case in which the smear detected a carcinoma that was missed on curettage and only demonstrated at hysterectomy was described.

Dr. Wachtel went on to comment: The fact that out of 133 proven cases of genital cancer 13, or roughly 10 per cent, were detected by the smear, and that other observers have had similar results, justifies the use of the method in routine gynaecological practice. It is in my opinion wrong to analyze the results only from the point of view of the percentage of cases of cancer detected in the total number of smear examinations, which is here about 0·18 per cent. The justification of smear investigation is found not only in the possibility of early diagnosis, but also in the opportunity of studying malignant disease at an early stage when its manifestations are still subclinical.

It is surprising that some observers state that the average time needed for slide screening is under 5 minutes. This is only true for the completely normal film in which the pattern is uniform throughout. In the vast majority of smears from gynaecological patients it is necessary to study the whole area of the film in detail, and this is hardly possible in 5 minutes. Speed and accuracy may be inversely proportional. This applies particularly to the recognition of malignant endometrial and ovarian cells, and to the differentiation between inflammatory and malignant changes in columnar cells. Single endometrial cells, the presence of which is always pathological except in the menstrual phase, is of gynaecological interest even in the absence of malignant features. They may be so interspersed with leucocytes that they may be mistaken for them unless a thorough screening of each cell is undertaken. Considering the factor of ocular fatigue in addition, it is hard to believe that anyone can look at and evaluate all the cells in a smear in 5 minutes. It would be a pity if cytologists themselves brought the method into disrepute by achieving speed at the expense of accuracy.

Carcinoma-in-situ is, in the majority of cases a cytological diagnosis, so far as the detection of malignant cells from a patient without symptoms or a macroscopic

lesion is concerned; but it is doubtful whether the appearance of the exfoliated cell will indicate the stage of the tumour from which it originated. The Americans claim that if the smear only contains well differentiated cancer cells this indicates non-invasive cancer, whereas a mixture of poorly differentiated cells means invasiveness. This is disproved by the fact that even with a histological diagnosis of non-invasive cancer in biopsy specimens, invasion can often be demonstrated later in the removed uterus. Cytological diagnosis is based purely on morphological appearances, and it seems wrong to deduce from the appearance of the visible exfoliated cell the behaviour pattern of the invisible non-exfoliated tumour cells left behind. The cytologist should not do more than give an opinion as to malignant and non-malignant cells, and leave speculation as to the extent of the disease to the surgeon and histologist.

Cytology has a place in the after-care of treated cases of malignant disease, and follow-up smears are a harmless method of investigation, though of course not infallible. We have no figures available to show the accuracy of this method, but it is reasonable to assume that the same accuracy applies as in the diagnosis of initial malignancies. Whether cytology has a place in the prognosis of radiation therapy remains to be seen. Dr. Wachtel thought that the claim that radiation response could be estimated by observing the proportion of benign cells showing radiation changes needed further investigation.

The impression had been gained during the study of smears from patients with uterine cancer that the oestrogen activity was unduly high. In a certain percentage of patients the oestrogen level drops sharply after treatment, whereas in others it remains high. It is possible that the persistence of oestrogen activity after surgical removal of the ovaries or their radiological destruction presents a bad prognostic omen, and it might be worth investigating this point.

MR. STANLEY WAY (Newcastle-upon-Tyne). Mr. Way said that the onset of symptoms in relation to the extent and curability of carcinoma of the cervix was so variable that even in cases in which there was no delay in instituting treatment cure was by no means certain. Cytology provided a means of detecting asymptomatic and really curable tumours which could not be detected by the naked eye or the examining finger. Cytology also provided the chief means of diagnosing intra-epithelial carcinoma and this was most important in view of the relationship of this disease to invasive cancer.

About 1 per cent of all gynaecological out-patients in whom no suspicion of cancer existed were found to be suffering from the disease when subjected to cytological examination. So far no cases had been detected by this means which were not small tumours limited to the cervix and without node involvement. This augured very well for the results of treatment in such patients.

The pressing need at the present moment was for research directed along lines which would reveal how best to use this method economically since it was clearly impossible to take smears from everyone. Since it had been shown that women whose smears contained a fairly high percentage of cornified cells after the menopause developed carcinoma of the cervix and the corpus more frequently than did women whose smears became atrophic, this type of patient would be worth following with routine smears.

The results of the treatment of carcinoma of the corpus were probably not as good as was generally believed and there was a good case here also for early diagnosis. Although the vaginal smear was not as accurate as in carcinoma of the cervix, the uterine aspiration smear was very accurate. Since women who reached the menopause after the age of 50 and also diabetics showed a high incidence of corpus cancer, a case could be made for routinely smearing such patients.

DR. A. S. WOODCOCK (University of Liverpool). In this centre, since commencement of the investigation 2 years ago, the time and labour involved in providing a routine diagnostic service have been particularly studied. This often neglected aspect appeared of considerable importance should cytodiagnosis come to be widely practised in this country, either in regional centres, or by individual clinical pathologists in general hospital laboratories.

Smears are obtained in the out-patient clinics of Sir Arthur Gemmell at the Women's Hospital and of Professor T. N. A. Jeffcoate at the Royal Infirmary. They are taken by members of the clinical staff from every new patient of 30 years or older, irrespective of signs or symptoms of disease, and provide material from between 1,000 and 1,200 patients per annum. Ayre's technique is used as it gives a concentration of fresh cells from the squamo-columnar junction of the cervix. When compared with the pipette method, its advantages of greater speed and at least equal accuracy in the diagnosis of carcinoma cervicis are considered to outweigh its unsuitability for the detection of carcinoma corporis. No difficulty occurs in making good smears with the spatula; less than one smear in 50 proves unsuitable for report. Special request forms of a "tick or cross out" pattern are used to secure adequate clinical information with a minumum of clerical effort. The smears are stained by a junior technician using Papanicolaou's method. This technician is also responsible for supplying the clinical departments with jars of fixative, spatulae and request forms. Rack and trough staining equipment is used, and it is found, with allowance for all the duties enumerated, that smears can be prepared for microscopy at the rate of 10 per hour. Simple charts of all the technical procedures are provided and a new and completely inexperienced assistant receiving very little direct tuition attained working proficiency within 3 weeks. All smears are reported by Dr. Woodcock, a pathologist claiming no specialized training to warrant the title "cytologist". The average reporting rate, carefully calculated, is 8 smears per hour. As a rule a rapid examination of the smear is sufficient to determine which of three broad patterns it presents: clearly benign, clearly malignant, or atypical with need for detailed study. The ease with which this classification can be made is considered a particular advantage of the smear obtained by spatula rather than pipette. Positive

smears are invariably confirmed or disproved by ring or cone biopsy. The cone has been preferred following a case in which this method revealed a carcinoma in a much scarred cervix after ring biopsy had failed to show the tumour.

The results in a random 1,000 consecutive cases were given:

(1) *Clinically unsuspected carcinoma cervicis.* Cases were only placed in this category if there had been no suspicion of significant abnormality on initial inspection and palpation of the cervix, and if following the positive smear a further thorough examination at the time of biopsy had been equally unrevealing. On this basis there were 5 examples of unsuspected carcinoma. On biopsy invasive carcinoma was found in 1 of these, and in 4 the appearances of carcinoma-in-situ. In another case unsuspected clinically the smear was reported as "doubtful", but on biopsy no carcinoma was found despite a thorough search of serial sections; this smear report must be regarded as incorrect—a "false positive" for purposes of assessment.

(2) *Clinically suspected carcinoma cervicis.* In 15 instances carcinoma was clinically suspected or obvious, and later proven by biopsy. In 14 of these (93 per cent) the smears were positive. In the remaining case, of a patient with a recurrence of cancer several years after radium therapy, no malignant cells were detected cytologically. This patient had vaginal stenosis which impeded accurate use of the spatula, and even after re-examination of the smear in the light of the biopsy findings no cancer cells could be identified.

(3) *Carcinoma corporis uteri.* No unsuspected cancers of the body of the uterus were detected in specimens collected by Ayre's method, and smears of this type were only reported as positive in 3 out of 6 cases suspected clinically and confirmed on curettage.

Dr. Woodcock went on to comment: The type of smear described is of little use in the detection of cancer of the body of the uterus but gives a reliable indication for biopsy in cancer of the cervix. Its particular value is to reveal early tumours before they are detectable by clinical examination. It appears from the present findings that some 5 such lesions can be discovered in every 1,000 patients by the use of smears. In terms of percentage this is a small yield, but in clinical values it consists of patients for whom the very early diagnosis offers prospects of successful treatment.

The scope of cytodiagnosis, however, is not confined to the discovery of unsuspected carcinoma. The negative report may be of value under circumstances in which the cervix is clinically suspect, but in which biopsy is, if possible, to be avoided; for example, in the case of lesions of the cervix during pregnancy. Equally in cases of cancerphobia a negative smear may provide reassurance for the patient. Cytodiagnosis is also a useful adjunct in the follow-up of patients who have received treatment for carcinoma. In the present investigation no attempt is made to assess immediate radio-sensitivity by smears, but they are useful as a later test for remaining or recurrent tumour.

The criticism is frequently made that the diagnostic return is small for the labour and time expended. The present service requires about 3 hours per week of the pathologist's time and 2 hours of the technician's. This moderate outlay is sufficient to maintain a rather greater turnover of cases than might be expected if cytodiagnosis were practised routinely throughout the gynaecological clinics of a large general hospital.

Moreover, there appears to be little justification for the tendency to regard diagnostic histology and cytology as very different crafts. Proficiency in the former is obviously not essential for proficiency in the latter, but the two are complementary, as Osborn (1953) has stressed, and the experienced histologist should rapidly acquire competence in the reporting of smears.

The effect of cytodiagnosis upon the histological services of the laboratory is important. A spate of "doubtful" reports must lead to an undue number of unfruitful biopsies, unnecessary to the patient and time-consuming to both clinician and histologist. In the present scheme it has rarely been found necessary to resort to an equivocal report. In the aggregate the number of biopsies incurred by "false positive" and "doubtful" reports is less than the number of instances in which mild clinical doubt is allayed by a firmly negative smear report, and biopsy consequently avoided.

In addition to their diagnostic uses the smears produce an accumulation of material on which to study the pathogenesis of carcinoma cervicis. In many biopsy specimens from clinically unsuspected cases the transition from normal epithelium to carcinoma-in-situ can be seen. In several, frank early invasive carcinoma is also present, so that the sequence from normal to undoubtedly malignant epithelium can be traced in one specimen.

The general policy has been to proceed to hysterectomy once a positive smear has been confirmed by biopsy. There have been instances, however, of lesions which were apparently non-invasive on careful study of ring or cone biopsy in which it appeared justifiable at least to defer removal of the uterus. One such patient who originally attended for investigation of her sterility was treated in this conservative manner. A positive smear was confirmed by cone biopsy, serial sections showing a non-invasive lesion. As the patient is most anxious to have a child she is being kept under observation, with further smears at 6-monthly intervals. A second patient, with a less extensive in-situ lesion at biopsy is under similar observation. Such cases may be a source of information when the theory of field origin of carcinoma is applied. This theory, well stated by Willis (1944, 1945, 1953) suggests that tumours arise from small or large fields of tissue in which a progressive neoplastic conversion may occur. Thus, although a particular carcinoma may appear non-invasive and completely contained within the portion of cervix removed at biopsy, the influences towards malignant change may still be operative in the remaining cervical epithelium. Repeated smears provide an opportunity for prolonged follow-up of these cases without unwarranted risk to the patient, and should aid in the assessment of the effectiveness of limited surgery for early lesions.

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Summary

by

Sir Arthur Gemmell and Sir William Gilliatt

Having taken considerable interest in gynaecological cytology for several years, having read the published work done in this and other countries, and having listened to the discussion on June 29th, we feel that we may be excused for expressing our opinion on the stage at which gynaecological cytology stands in the British Isles today. It may be said that cytology is practised in several centres (here are reports from nine) with regularity, as in some clinics all patients over 30 years of age attending gynaecological out-patients have smears taken, and in many more centres on a less constant scale. It will be obvious therefore that work in this Country is many years behind that in North America, particularly in the United States, where cytology is accepted as a method of diagnosis of both carcinoma of the cervix and of the corpus of the uterus. We believe that it is impossible in the present state of our knowledge, and of our experience in cytology, to accept a positive smear as establishing the diagnosis of malignant disease, but it is a compelling sign that further detailed investigation is urgently called for to confirm or disprove the suspicion which a positive smear produces. If cytology is regarded in this manner then mistakes will be avoided which arise if reliance is placed upon it as a method of diagnosis complete in itself.

We feel that the most important thing to extend the use of cytology in gynaecology is enthusiasm in either the clinician or pathologist—preferably in both—which is of such a degree as to be infectious. It is agreed by most workers that gynaecological cytology should be a part of general cytology which should be carried out in the pathological departments so that the cytologist and histologist, both so necessary in the cytological field, are always working in close proximity.

We believe that it is desirable to extend gynaecological cytology by gradual and methodical steps in a limited manner with definite safeguards. The first essential step towards the establishment of a cytological centre is the creation of an efficient and enthusiastic team (sometimes called a Study Group) to carry out the work. In the above reports it will be seen that teams have been formed on two broad plans. The active and enthusiastic co-operation of clinician and pathologist is an integral part of both. In one type they are assisted by a team of technicians trained in cytology who undertake screening of the smears. In the other, the pathologist himself examines all smears which have been stained by trained laboratory workers. We realize that cytologists and technicians both require a long training but so do other workers in pathological departments.

We also believe that it is undesirable to suggest that *all* women should be offered regular smears as is done in some countries.

The material here presented from this country has been collected from different sources, by far the most common being from patients attending gynaecological out-patient departments, whether there is clinical suspicion of malignant disease or not. Experiments have been carried out by taking smears from all patients attending

(*a*) Cancer Prevention Clinics.

(*b*) Contraceptive Clinics.

In each of these the work was found to be tedious and unrewarding and was stopped as soon as this result was shown early in each experiment.

There is no doubt, as will be seen by reading the foregoing reports of those who work in cytology, that they at least are certain of its value. Indeed, from those reports recording them, we have extracted figures showing the percentage of unsuspected cancers discovered by cytology alone, in the total number of uterine cancers dealt with in the departments from which smears are obtained:

Total number of cases of uterine cancer 420

Number detected by smear alone .. 56=13 per cent

This figure means that for every 364 cases of uterine cancer in various stages of the disease that can be diagnosed clinically, the smear method has added 56 cases, each one of which is in the earliest stage of the disease, a stage in which a very high percentage of permanent cures can justifiably be expected.

NEWCASTLE-UPON-TYNE OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

October 1955

A Meeting of the Newcastle-upon-Tyne Obstetrical and Gynaecological Society was held on Thursday, 13th October, in the Royal Victoria Infirmary, Newcastle-upon-Tyne. The President, Dr. Cosgrove, was in the Chair.

Professor C. H. G. Macafee gave an address on

The Changing Face of Obstetric Practice and Teaching

Professor Macafee said that the art of obstetrics was age old but many changes had taken place in the science and practice of the art, especially in the last twenty-five years. He did not wish to discuss such outstanding changes as the introduction of chemotherapy, the use of blood transfusion, improved anaesthesia and the general raising of the standard of obstetric care. All these had combined to produce a reduction in foetal and maternal mortality.

Obstetric practice, for generations the concern of the family doctor, had in some areas again fallen into the hands of midwives until in England and Wales about 80 per cent of the cases now came under their care. Consultant practice, too, had altered over the same period. In former times the family doctor referred only those

cases in which he anticipated abnormality or undue difficulty and these often at a late stage in pregnancy. For a number of years it had become customary for the family doctor to refer every type of case from the earliest weeks of pregnancy. Possibly two factors could be cited as a reason for this change.

In the first place before the last war many family doctors had given up or materially reduced their midwifery practice. Such doctors chose to refer their cases either to hospital or to a consultant rather than to another family doctor.

The second important influence was the demand on the part of the general public for institutional midwifery either public or private rather than for the traditional domiciliary confinement.

The National Health Act of 1948, however, had tended to encourage the resumption of domiciliary practice but how far the pendulum would swing remained to be seen.

In his opinion, if the family doctor wanted to return in strength to the obstetric field then this was his opportunity provided he recognized his responsibilities, appreciated the changes that have occurred and equipped himself accordingly.

From the point of view of the obstetrician, whether consultant or family doctor, certain notable changes in the clinical course of pregnancy and labour and the increased facilities for additional help if necessary had made obstetrics an easier if not less exacting branch of medicine.

When Ballantyne instituted prenatal care he opposed the notification of pregnancy, but he thought "that a small sum of money might usefully be offered to women giving early notice of confinement". This principle of bribery had been employed in a more subtle fashion in recent times. The introduction of a bill before Parliament to make the notification of pregnancy compulsory would almost certainly have met with defeat, but during the last war the necessity for making arrangements for the confinement early in pregnancy and the lure of extra rations and clothing coupons tore the veil of secrecy to ribbons. Gone was the false modesty of the Victorian and Edwardian eras. The expectant mother today not only notified her doctor but also her butcher, grocer and milkman.

This altered attitude of the patient towards pregnancy was, he believed, one of the important advances of our time and might be responsible, among other things, for the noticeable decrease in hyperemesis gravidarum.

The pregnant woman of today realized the value of antenatal care and did not hesitate to present herself at an early stage for supervision by her doctor or nurse. The regular supervision by her attendant was also of inestimable psychological benefit to the patient and rapidly established a mutual understanding from which the patient derived confidence, an essential factor in the successful outcome of labour.

The medical advantages of antenatal care were too well known to require elaboration. It was regrettable that on many occasions so-called antenatal care was poor and of such a standard that the benefits both from the psychological and medical aspects were lost. This criticism applied to both hospital and private practice. In hospital the clinics were too large, too busy and too hurried for time to be given to the psychological approach.

On the other hand, the patient admitted with eclampsia who had not had her urine tested for three weeks might have complete confidence in her doctor, but had obviously not received good antenatal care.

The noteworthy fall in maternal mortality and the more general use of sedatives and analgesics had done much to allay the dread of childbirth in the mind of the lay public. This brought Professor Macafee to the next noteworthy change—the alteration in the clinical course of labour. The duration of labour in primigravidae had become appreciably shorter in the last 20 years. For a number of years he had taught that if a primigravida was not approaching the second stage of labour at the end of 12 hours one should review the case most carefully to see what factor or abnormality had been overlooked.

That the duration of labour at first confinements had shortened was not entirely a personal observation as it had been mentioned to him on several occasions by family doctors.

In order to confirm this clinical impression he reviewed for the purpose of this paper approximately 3,000 case sheets of patients delivered in the Royal Maternity Hospital, Belfast, and private patients whom he had attended personally in the private block of this hospital.

He showed that since 1938 the average duration of labour in the private primigravida had been reduced from just over 19 to just under 13 hours. It would therefore appear that the normal primigravida of today could expect a duration of labour which her grandmother or mother could only hope for at her second or third confinement. Even in the hospital patients there was an appreciable reduction in the duration of labour in spite of the high proportion of associated obstetrical or medical complications.

He could not agree with the statements in textbooks regarding breech presentation. It was his belief and experience that the breech was a good dilator, particularly when the legs are extended, and when the breech delivery was going to be successful *per vias naturales* the duration of labour was shorter than in the normal vertex presentation. Moderate or severe disproportion of course could interfere with the progress of labour in the breech presentation just as it did with a vertex presentation. He believed that, when one was supervising the primigravida with a breech presentation, the case must be reviewed at the end of 8–10 hours of labour if the first stage was not completed or almost completed. He therefore could not endorse the statements in *Midwifery by Ten Teachers*. "The Course of labour may be prolonged and difficult especially in primigravidae for the following reasons:

(1) The breech is less efficient than the head in dilating the cervix and stimulating uterine contractions.

(2) The extended breech undergoes lateral flexion with some difficulty because of the splinting effect of the extended legs . . ."

Professor Macafee said that it had also stated that the foetal mortality was greater when the legs were extended, but Stabler had shown that extension of the legs was found in the majority of breech presentations.

Mr. G. B. Gibson, lately his University Lecturer, had investigated the duration of labour in a large series of breech presentations delivered in the Royal Maternity and Jubilee Maternity Hospitals, Belfast. He had found that the average duration of labour both in primigravidae and multiparae delivered *per vias naturales* was exactly the same, namely, *eleven* hours. In view of this finding Professor Macafee considered that a trial of labour in breech presentation was justified in the absence of other obvious complications such as gross pelvic contraction. If the labour was going to terminate easily and successfully *per vaginam* then the uterine contractions occurred regularly, the cervix dilated rapidly, and the breech descended on to the pelvic floor. Contrary to the teaching already quoted the presence of extended legs was an advantage rather than a disadvantage especially in a primigravida.

He had recently learnt that the late McIntosh Marshall since 1945 had advocated trial of labour in breech presentation. Cox (1955), one of Marshall's pupils, stated that "trial of labour in the modern sense, where progress is assessed after some hours of strong uterine contractions, is quite reasonable. If the breech engages in the pelvic brim, the cervix dilates rapidly, and full dilatation occurs within the normal duration of labour, the outcome will be favourable." He could only say how strongly he supported these views but would be inclined to put a time limit of 12 hours on the duration of labour.

He drew attention to the following sentence in the last edition of *Operative Obstetrics* by Munro Kerr and Moir: "The personal experience of the obstetrician is the most important single factor in determining the safety or otherwise of the breech delivery." In the event of a stillbirth at a breech delivery it only required a cantankerous husband and an able lawyer to use that sentence as the occasion to make every breech in a primigravida a possible legal liability. A breech delivery in a primigravida should be conducted with all available assistance and preferably in a well-equipped institution because there was no doubt that a higher proportion of these cases required skilled intervention.

Why the duration of labour had diminished was hard to say. There were probably many factors accounting for this change but it was possible that the most important was one which he had already mentioned, that is, the altered attitude of the patient herself towards pregnancy and labour.

The past 20 years had seen the gradual disappearance of a misconception, prevalent among the lay public and some members of the medical profession, that every qualified practitioner was sufficiently trained to carry out singlehanded any obstetrical operation. Now, if he should seek the assistance of an anaesthetist or a consultant colleague, it was not regarded as a reflection on his skill but rather as evidence of his good judgment. In the home of the "Flying Squad" one did not need to discuss the value of additional help in domiciliary midwifery. This service was now almost a national institution which Newcastle must be very proud to have inaugurated. The number of lives which have been saved as the result of it could not be assessed.

There was no excuse nowadays for failed forceps, for making vaginal examinations on cases of ante-partum haemorrhage in the patient's own home or for trying to deal with malpresentations singlehanded. The consultant service was available and should be utilized.

The next noteworthy change was the improved facilities for dealing with complications associated with the third stage of labour. The discovery of ergometrine, the availability of a Flying Squad in almost every area and the liberal supply of blood had relieved many doctors of the anxiety associated with the third stage in the past. However, it was regrettable to find that in the Registrar General's Report (1953) 51 women, or almost one woman per week, died from post-partum haemorrhage in England and Wales. How much longer would it be before post-partum haemorrhage was eliminated from the maternal mortality figures?

The virtual disappearance of puerperal sepsis since 1937 had removed one of the great bugbears of obstetric practice. There were indications, however, that the return of this scourge was not beyond the bounds of possibility.

The abuse of antibiotics by all branches of the profession had now produced so many resistant organisms that the risk of sepsis was as great as ever if our aseptic and antiseptic precautions were relaxed.

Occasionally one saw a case reminiscent of the days when puerperal sepsis was common and here the termination was as fulminant as ever even with antibiotic treatment. It might not be significant, but in England and Wales in 1952 61 women were recorded as having died from puerperal sepsis. In 1953 there were 71 such deaths.

It was difficult to impress the dangers of puerperal sepsis on students and junior resident staff. Many of them had never seen cases of puerperal sepsis with which doctors of his generation were only too familiar and they sometimes tended to be careless regarding their aseptic technique because they felt that antibiotics would cure any infection. He would not like the audience to think that he did not approve of the use of antibiotics but he felt much safer if he did not require to use them. There had been many complications and even fatalities associated with their use and abuse.

The changes mentioned had altered the outlook of the obstetrician, both the consultant and the general practitioner. While it was a fact that avoidable maternal deaths still occurred and a further reduction in the maternal mortality rate was possible it was gratifying to realize that this rate was approaching an irreducible minimum.

Greater attention was now being paid to associated medical diseases, e.g., anaemia and cardiac disease, and to reducing the number of stillbirths and neonatal deaths. Neonatal deaths were to a large extent the concern of the paediatrician, but the obstetrician must

endeavour to avoid providing them with an impossible task. If the numbers of grossly premature infants could be reduced then modern paediatric nursing technique could work wonders.

Intra-uterine and intra-partum deaths were most frequently associated with hypertension, toxaemia, ante-partum haemorrhage and rhesus incompatibility. Much had been done to reduce the foetal mortality but more could be achieved.

Pre-eclamptic toxaemia had been associated with a high foetal mortality partly on account of the risk of intra-uterine death, but also as the result of premature induction of labour. It had been taught that it was a mistake to prolong the pregnancy for more than 3 weeks from the onset of toxaemia because of the risk of permanent damage in the nature of chronic renal disease or persistent hypertension.

Since 1945 he and his colleagues had not subscribed to this view and they had endeavoured to carry on pregnancy to as near term as possible. From 1946 to 1950 there were 1,420 cases of pre-eclamptic toxaemia, hypertension and chronic nephritis treated in the Royal Maternity Hospital, Belfast. Of these cases 1,355 had been reviewed by Mr. Gibson and himself, and from the follow-up it would appear that evidence suggesting permanent residual damage did not depend on the severity of the toxaemia or on the duration of treatment between the onset of toxaemia and the induction of labour.

TABLE I
Percentage Incidence of Chronic Renal Damage or Persistent Hypertension

Less than 7 days treatment	25·8
7–13 days treatment	34·4
Over 13 days	32·8
Mild cases	25·0
Moderate cases	34·1
Severe cases	32·6

Evidence of permanent residual damage depended on the presence of hypertension and/or albuminuria 3–5 years after the pregnancy which was associated with toxaemia.

The time at which labour was induced did however seem to have some bearing on the foetal mortality rate. From figures already published by Mr. Gibson it appeared that in the interest of the baby it was safer to induce labour somewhere between 35 and 37 weeks. If one tried to carry on a toxaemic pregnancy to 39–40 weeks there was a gradually increasing foetal loss.

When one considered ante-partum haemorrhage one found that as far as placenta praevia was concerned much had been done all over the United Kingdom to reduce both the foetal and maternal mortality associated with this complication.

From Table II it could be seen that there was still room for improvement. Too many cases of placenta praevia were still being treated too early to secure viable babies and this was partly due to the patient being submitted to a vaginal examination before admission to hospital.

TABLE II
Mortality in Placenta Praevia

Author	Number of Cases	Foetal Mortality	Maternal Mortality
		(Per cent)	(Per cent)
Berkeley (1936) ..	4,580	59·0	7·0
Browne (1944) ..	3,103	54·0	5·9
Macafee (1954) ..	1,553	22·9	0·9

Table III compared the results from a hospital where a high percentage of cases received conservative treatment with those where the percentage was lower.

To show that these 70 cases were not loaded favourably with mature babies he pointed out that 25 of the 70 patients, or more than one-third, had had their first

TABLE III

Group	Number Receiving Conservative Treatment	Foetal Mortality in Cases Treated Conservatively	Maternal Mortality in Cases Treated Conservatively
	(Per cent)	(Per cent)	(Per cent)
1553 ..	257 (16·5)	14·7	0·79
1353 ..	187 (13·8)	20·8	1·07
200 (R.M.H.)	70 (35·0)	8·5	0

haemorrhage before the 30th week. The minimum time between admission and treatment of these 25 patients was 12 days and all were delivered of live babies. Unfortunately, 3 of these babies had died in the neonatal period, but even in this unfavourable group the foetal mortality was only 12 per cent.

Of the 200 cases treated in the Royal Maternity Hospital from 1946 to December, 1953 the uncorrected foetal and neonatal deathrate was 12 per cent. The details of these 200 cases were published by Dr. Grant from his Department in the August number of the *Journal of Obstetrics and Gynaecology of the British Empire* (1955). He understood from Mr. Stallworthy that in Oxford they had managed to reduce the foetal mortality to 10 per cent.

The Belfast figures had been obtained by close co-operation with the family doctors. They knew that they had only to say that their patient had had an ante-partum haemorrhage to secure her admission to hospital, however acute the bed situation might be. Following her admission it was the obstetrician's responsibility to decide for how long that patient must remain.

This service had never been abused but he would prefer to have it abused rather than have the patients examined vaginally before admission.

Though it was not strictly relevant at this stage he wanted to point out the improvement in the Maternal Mortality, in association with placenta praevia, which had taken place over the years from 1942–1952 as

illustrated from the Table of the Registrar General's reports:

TABLE IV
Placenta Praevia—England and Wales

Year	Total Deaths	Deaths During Pregnancy	Deaths During or After Labour
1942	68	10	58
1943	64	11	53
1944	66	10	56
1945	50	6	44
1946	60	15	45
1947	41	5	36
1948	36	3	33
1949	22	6	16
1950	24	9	15
1951	29	3	26
1952	15	1	14
Total ..	475	79	396

He regretted to say that in 1953 according to the Registrar General's report 33 women died in England and Wales as a result of ante-partum haemorrhage due to placenta praevia.

While some progress had been made in dealing with placenta praevia it was another story when accidental haemorrhage was considered. He was indebted to Dr. Grant of his own Department for the following, as yet unpublished, figures.

In the years 1943–1951 inclusive there were 360 cases of accidental haemorrhage treated at the Royal Maternity Hospital. Of these cases 115 or 31·9 per cent were of the toxic and 245, or 68·1 per cent, of the non-toxic type. From Table V it could be seen that accidental haemorrhage of either type was more serious for the baby than placenta praevia treated on modern lines.

TABLE V
Accidental Haemorrhage (360 Cases)

Type	No. of Cases	Per-centage	Foetal Mortality	Recurrent Haemor-rhage
			(Per cent)	(Per cent)
Toxic ..	115	31·9	73 (63·5)	25
Non-toxic	245	68·1	67 (27·3)	29

He therefore disagreed with those who advocated placentography in all cases of ante-partum haemorrhage with the object of allowing the patient to return home if a placenta praevia or toxic accidental haemorrhage could be excluded.

Percival and Murray in a recent paper in the *Lancet* stated "Soft tissue placentography can greatly reduce such use of valuable beds; in non-toxic accidental haemorrhage once placenta praevia has been excluded and bleeding has ceased the patient can safely be sent home".

When one saw that non-toxic accidental haemorrhage was associated with a foetal mortality of nearly 30 per cent and that 29 per cent had recurrent haemorrhages it was surely essential that these patients should be admitted for careful assessment. In a recent review of the foetal mortality in the Royal Maternity Hospital, Belfast, the two varieties of accidental haemorrhage accounted for one-third of the babies lost.

In Professor Macafee's experience the greatest advantage of accurate placentography was to diagnose the situation of the placenta before haemorrhage had occurred or where the amount of blood loss had been small. Placentography would frequently fail to demonstrate the presence of a placenta membranacea in the lower segment and he had allowed a patient to go home on the strength of placentography and a head engaged in the pelvic brim only to have her re-admitted a few days later with ante-partum haemorrhage and requiring a Caesarean section.

Teaching

How have these changes in practice affected the teaching of the subject?

The ideal method of training the student he believed was to allocate antenatal patients to him so that he could follow them through labour and the puerperium. This of course was only possible in a modified way while the student was in residence. He thus gained the maximum benefit of seeing the patient in all stages. In many cases, however, the first occasion on which the student saw the patient was at the termination of the second stage which allowed him to count a case without learning very much.

Few would disagree that the foundation of the Royal College of Obstetricians and Gynaecologists in 1929 was one of the greatest influences in improving the standard of obstetric practice and teaching not only in the United Kingdom but throughout the Commonwealth.

While the College had advocated 90 per cent institutional confinements there were many who would not agree with this attitude and who still believed that for the normal case a domiciliary confinement was not only happier for the mother but safer for the child. It was possible that for a long time there would be a high percentage of domiciliary confinements. How was the student and the recently qualified practitioner who was studying for his diploma to acquire experience in domiciliary midwifery? The National Health Service Act to a large extent abolished the district midwifery associated with teaching hospitals and thus removed a valuable source of clinical experience and training which the student and resident doctor could acquire. Could this source of training be replaced? He believed it could and that was where the family doctor could play a most important part as member of a University departmental team.

Three years ago he had suggested that the University should enlist the assistance of a certain number of family

doctors who had large domiciliary midwifery practices to help in the training of medical students. This advice was accepted by the Senate and Academic Council and four family doctors were appointed as clinical lecturers.

These doctors had been most co-operative and helpful in taking students out to district cases although to do this had meant a great deal of extra time and trouble on their part and he had feared might make too great a demand on their already overcrowded days. Fortunately the family doctors were men whose standard of work was high, whose methods were good and capable of adaptation to the existing circumstances and who were never afraid to ask for advice though they rarely required it. The reaction of these doctors to the scheme was surprisingly good. They stated that although this added considerably to the amount of work and time expended they not only enjoyed doing it but learnt a great deal from the students. They stated that they had to renew their knowledge of the textbooks to their great advantage. Their other comment was that the presence of the student was a great advantage to them personally because in the event of any unforeseen complication the doctor had an additional pair of responsible hands upon which he could call either for assistance or to secure assistance. The doctors also felt in a more secure position as they had all the resources of a teaching hospital behind them and naturally those working in the hospital appreciated their increased responsibility to these doctors.

The students were most appreciative not only of the experience, limited though it necessarily must be, but of the trouble that the doctors took to help and teach them. It had been most interesting to watch the relationship between the student and the family doctor gradually develop until now the student was regarded and treated as a useful member of the family doctor's team.

Each year before the student began his practical midwifery course one of the four doctors gave one or more lectures on midwifery in general practice to the large systematic lecture class. In these lectures the doctor not only covered the purely practical aspect of antenatal care and conduct of labour, but told the student about the family doctor's relationship with hospitals and public health authorities. In this way the student got an insight into the pleasures and difficulties of general practice at an early stage and could appreciate the position of the family doctor when he became a resident doctor in hospital.

In addition to the family doctors he had had the benefit of the help of a doctor from the Public Health Department working with him in the antenatal out-patient clinic and a Health Visitor who went round the lying-in ward with him and the Professor of Child Health once a week. This allowed him to secure many of the facilities which the Public Health Department provided such as instruction on mothercraft, breast feeding, relaxation exercises and the after-care in co-operation with the patient's own doctor. The doctor from the Public Health Department also instructed the students in residence and took them to her own antenatal clinics in other parts of the City.

The qualified house officer did not get much opportunity even now of having to deal with normal domiciliary midwifery but experience with the Flying Squad did give him a certain insight into domiciliary obstetrics.

The ideal would be to be able to second a house officer to work with a family doctor, who practised obstetrics, for say three months so that he could get experience of the methods which must be employed in such circumstances. Then he must be able to adapt the methods and facilities to which he had become accustomed in hospital to the altered surroundings in the patient's own home.

The members of his Department were most grateful to those family doctors who so willingly co-operated in this scheme of training students. The experience gained in dealing with them had been most valuable and after all, whether consultants or family doctors, our object was the same, to work together for the good of the patient and the advancement of our art.

In the modern antenatal ward the student should be able to add to his knowledge of general medicine. On a recent occasion in his own antenatal ward there were patients suffering from megaloblastic anaemia, Addison's disease, chronic nephritis, congenital cystic kidney, diabetes, cardiac disease, hypertension, cerebral tumour, and in a separate ward in the same hospital were pregnant women suffering from pulmonary tuberculosis.

If such cases were allocated to students and discussed on ward rounds with the other members of the small resident class it would be a valuable addition to their general medical training.

The altered attitude towards the treatment of obstetric complications in domiciliary midwifery had made a difference in what students are or should be taught.

More stress is now laid on normal labour. If the student or doctor could recognize at an early stage the departure from normal and was prepared to recognize his operative limitations and seek assistance early, fewer stillbirths and damaging deliveries would result.

This change in teaching had led to the view that doctors who intend to practise obstetrics in general practice should have postgraduate training in this branch of medicine.

While this view had no legal support it was one which, to a large extent, was supported by the younger members of the profession and of course by the Royal College of Obstetricians and Gynaecologists. The College instituted its diploma with the express object of conferring upon those doctors who had acquired this extra training a diploma whereby they could be recognized.

In the teaching of undergraduates there was still not enough supervision of the students training by members of the University departments. This applied more to the large than to the small medical school. In the schools which could provide all the clinical training for their students it was impossible for the Head of the Department and his team to be responsible for what was taught when his students must go to other hospitals, perhaps outside his own city, to receive their training in practical obstetrics.

There was a tendency among some teachers and many students to regard obstetrics as a question of delivering a baby and placenta. Students and teachers sometimes

forgot that pregnancy was a most interesting physiological process closely allied with medicine, the management of labour might require great judgment and at times operative dexterity, and the puerperium with the addition of the baby had its own interests.

In 1936 Farquhar Murray read a paper entitled "Whither Midwifery?" At the beginning of his paper he made the following statement:

> "Anyone on the staff of that peace-time casualty station, the maternity hospital, has abundant evidence that many pregnant women do not get proper medical supervision, that many recently delivered women do not receive adequate nursing and that there is a deplorable lack of co-ordination and co-operation between the medical and nursing services concerned."

He finished up by saying:

> "What has been done at Newcastle can be done in any other medical school centre."

It must give Murray and his colleagues great pleasure to see how many of the things done at Newcastle had been copied all over the country.

Of recent years great political capital had been made out of the improved maternal and infant mortality. If credit for this improvement was to be given it should be to those whose work brought about improved control of sepsis, to those who introduced the sulphonamides and antibiotics and in no lesser degree to midwives, family doctors, obstetric specialists and teachers who, each in his sphere, had contributed to the welcome and steady improvement which has occurred in the last twenty years.

As St. John Irvine had said recently:

> "A finer race will be raised by those who desire it, but it will not be created by those who have subjected themselves to slavers, whether the slavers be private persons or Government departments. The beginning of all improvement is made by individuals."

FÉDÉRATION INTERNATIONALE DE GYNÉCOLOGIE ET D'OBSTÉTRIQUE

INTERNATIONAL FEDERATION OF GYNECOLOGY AND OBSTETRICS

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The objects of the Federation as stated in article 2 of the Constitution are:

"(*a*) To promote the development of science and assist in scientific research work relating to all the fields pertaining to gynecology and obstetrics, to further the attainment, by all appropriate means, of a higher level of physical and mental health of women, mothers and their children, to develop and improve the exchange of information and ideas in the field of gynecology and obstetrics, to contribute to the research of fresh knowledge in this field, to contribute to the improvement of teaching standards in the profession, to promote international cooperation and facilitate relationships between national medical bodies of the profession.

"(*b*) To recommend a common policy in regard to these matters on the proposal of member societies.

"(*c*) To represent member societies whenever joint scientific action can be pursued in such matters.

"(*d*) To foster the initiation and development of all activities aiming at the attainment of the objects of the Federation as defined under (*a*) above.

"(*e*) To organize international congresses including all countries or certain groups of countries. Circumstances permitting, each international congress shall be held successively on a different continent. Members of national societies may attend all congresses."

BOOK REVIEWS

"Atlas der Kolpomikroskopie (Atlas of Colpomicroscopy)." By PROF. DR. TASSILO ANTOINE and PRIV. DOZ. DR. VIKTOR GRUENBERGER, Vienna. Pp. 244, 176 photomicrographs, 35 references. Georg Thieme Verlag, Stuttgart, 1956. Price DM 64.

THE two great recent advances in early cancer diagnosis of the uterus are represented by the introduction of cytology by Papanicolaou and Traut, and colposcopy by Hinselmann. Antoine and Gruenberger have further developed colposcopy into colpomicroscopy, introducing the incident light technique and thus permitting greater magnifications of the examination field. Ordinary colposcopy magnifies 10–40 times, whereas the colpomicroscope can produce nearly 10 times higher magnifications (×110–280). Colpomicroscopy, therefore, equals ordinary microscopy and has the advantage over histology that it deals with living tissues which can be observed repeatedly. As the authors themselves put it in their concluding remarks: "Histology gives you a single snapshot, colpomicroscopy a cine film."

Colposcopy and colpomicroscopy are essentially German and Austrian inventions and the rest of the world is only slowly realizing the value of these forms of investigation. In order to make their book more available and increase its circulation the authors had the original idea of writing the main parts (methods and text illustrations) in three languages, viz., German, English and Spanish. It is, however, a great pity that the execution of this excellent idea seems to have suffered from the lack of an expert translator.

The authors confine themselves to a very short theoretical part in which they describe the history of the colpomicroscope, the development of the instrument and the instrument itself, examination technique, staining methods, colpophotomicrography and the common appearances of the cervix under the colpomicroscope. The theoretical part, including the translations, comprises only 18 pages. The rest of the book is devoted to illustrations.

Normal and abnormal epithelia are shown as colpophotomicrographs and are compared with the corresponding histological sections. The choice and technical perfection of these pictures are admirable despite the natural restrictions inherent in the method such as the impracticability of its use in cases of rigid inflexible cervices, stenosed vaginae and in the presence of blood.

In addition to the use of the colpomicroscope in the living patient, the method has been recently applied successfully to the examination of operation specimens and compares favourably with "the frozen section" technique. Relevant reproductions of colpophotomicrographs of endocervical, endometrial, parametrial and ovarian tissues are shown.

Finally, the authors show colpophotomicrographs illustrating studies of cyclical changes in the cervix and changes occurring during pregnancy.

This unpretentious book with its wealth of illustrations represents many years of laborious and painstaking study. It is a fascinating and impressive work and, probably, a most important foundation for a new field of medical advance.

Erica Wachtel

"Grundriss und Atlas der Gynaekologischen Cytodiagnostik (Outline and Atlas of Gynaecological Cytodiagnosis)." By H. SMOLKA and H. J. SOOST. Pp. 166, 186 photomicrographs, 6 tables, 409 references. Georg Thieme Verlag, Stuttgart, 1956. Price DM 120.

CYTOLOGY has come a long way since the publication of Papanicolaou and Traut's book on *The Diagnosis of Uterine Cancer by the Vaginal Smear* in 1942. Detection of malignant cells in vaginal smears is now only one aspect of gynaecological cytology; other equally important applications are to be found in the endocrine field and in cytological control of response to treatment of malignant disease.

Smolka and Soost have attempted to tackle all problems with which the gynaecological cytologist is confronted and they deserve praise for their precise and accurate mastering of the subject. After discussing smear techniques and laboratory methods they describe the various constituents of vaginal smears, smear patterns in different age groups, cyclical variations, pregnancy, puerperium and lactation, changes in pattern after hormonal administration, hormonal deficiencies and excesses, specific and non-specific inflammatory patterns, cancer diagnosis and cell changes after radiation therapy and finally advice on the organization of a cytological laboratory. They illustrate each chapter with appropriate photomicrographs, many being excellent colour reproductions, and end their book with an almost complete list of the main references in cytology.

The brevity of the book is at the same time commendable and a shortcoming. It provides an excellent survey of current cytological techniques and views, but is not quite detailed enough as a beginner's introduction into the field of cytology. It provides, however, a first-class reference book for the expert as well as an invaluable source of information to the gynaecologist regarding the aids cytology can give him in gynaecological problems.

Erica Wachtel

"A Short Textbook of Midwifery." By G. F. GIBBERD, M.B., M.S., F.R.C.S., F.R.C.O.G. 6th edition. Pp. 593, 199 illustrations. J. & A. Churchill, Ltd., London, 1955. Price 30*s*.

AFTER an interval of four years, this popular textbook

reappears in its sixth edition. A new preface refers to the subtlety of most of the recent changes in obstetric practice. Revision has been completed with the addition of 17 pages, and it has evidently been most thorough. Needless to say, this sterling British textbook continues to inspire a well reasoned approach to obstetric problems while reflecting the ripe judgment of its author.

A new section deals with postmaturity. It is advised that where the mother's statement about the date of her last menstrual period is vague, or if her menstrual cycle is sometimes prolonged to six weeks or more, it is not possible to do more than guess at the duration of gestation within three or four weeks even with the aid of the time of first perceptible foetal movements, the time of appearance of centres of ossification, cephalometry and the size of the uterus. In such cases it is wiser not to make a clinical diagnosis of postmaturity. The effect of increasing size and hardness of the foetal head on the outcome of labour is discussed and the danger of anoxia from progressive placental insufficiency is considered in relation to the management of postmaturity. The conclusion is that the risks of induction of labour may exceed the hazard of anoxia from placental insufficiency. It is preferable, in general, to await the spontaneous onset of labour, which should be managed with due regard to the special risk of foetal anoxia. In cases of doubt such as a trial of labour "the extra hazard of postmaturity may easily swing the balance in favour of Caesarean section".

The chapters dealing with toxaemia, uterine inertia, puerperal infections, ante-partum haemorrhage and haemolytic disease of the newborn have been extensively revised. There is little change in the placenta praevia section; the advantages of conservative management are presented. In the summary of management mention is made of digital vaginal examination in hospital a day or two after bleeding has ceased when "in the unlikely event of the cervical canal being dilated the diagnosis can be made at this stage"; elsewhere it is clear that the author does not intend to advocate such premature interference. Later, it is stated that "if there is any suspicion that the placenta may be centrally placed it is a safe precaution" to examine the patient in a theatre prepared for Caesarean section; it is not clear how the author can guess at degrees of placenta praevia or proceed to explore the lower uterine segment with any less precaution. Other points of note are that preparations for blood transfusion if required are not clearly stated to be obligatory before the diagnostic examination is made; the specification of a 2-finger examination in diagnosis; the personal preference for the upper segment operation when section is required. In the otherwise admirable section on accidental haemorrhage, it is disappointing that no reference is made to disorders of blood coagulation in certain cases of grave risk.

In the clinical classification of the toxaemias of pregnancy the term pre-eclamptic toxaemia has replaced albuminuria of pregnancy in deference to popular usage. Special consideration is given to differentiation between pregnancy with chronic renal or vascular disease and pre-eclamptic toxaemia. Alternative views on these controversial matters are stated; the author remains convinced that in certain cases the development or worsening of hypertension may occur as a legacy of pre-eclampsia in a woman previously free from vascular or renal disease.

In dealing with pelvic tumours complicating pregnancy, surgical removal between 12 to 20 weeks is recommended but it is not clear whether examination of all patients at an early stage of pregnancy, to ensure timely detection of smaller tumours, is advised. There is some conflict, also, between the advice that the ovarian cyst discovered late in pregnancy should be removed as late as the second or third week of the puerperium with the later advice that the risk of torsion after delivery calls for removal early in the puerperium.

Despite these criticisms of certain detail, the new edition maintains the high standard of its predecessors. Lack of space inevitably limits the scope of the work. Nevertheless, it is compact of well selected information and good sense in an agreeably balanced presentation which will ensure its continued success.

"Midwifery: Principles and Practice for Pupil Midwives, Teacher Midwives and Obstetric Dressers." By R. CHRISTIE BROWN, M.S., F.R.C.S., F.R.C.O.G., BARTON GILBERT, B.Sc., M.D., F.R.C.S., F.R.C.O.G., DONALD B. FRASER, F.R.C.S., F.R.C.O.G., and RICHARD H. DOBBS, M.D., F.R.C.P. Fourth Edition. Pp. viii+892. With 223 figures. Edward Arnold, London, 1956. Price 25*s*.

NINE hundred pages from four authors for five crowns is excellent value at any time; when quality is as evident as quantity, the result is nothing less than a bargain. That this has been appreciated is shown by the fact that there have now been 11 printings of four editions since this book was first published in 1940. Two new chapters, one on antenatal paediatrics and the other on ovarian and placental hormones, bear witness to the progressive approach of the authors, whose avowed aim is to teach the reader to think rather than to memorize. A notable feature of the book is the introductory sections of short succint chapters on scientific principles and on general anatomy and physiology. The text is generally sound and modern in teaching, but the anomalies of uterine action might be more lucidly expounded, and it is not in the interest of the midwife to perpetuate the distinction between primigravid and multigravid breech delivery. Similarly, the advocacy of sedation for inertia in the second stage of labour is of doubtful wisdom. However, these are matters of opinion, and the book can be wholeheartedly recommended, particularly as a reference book for teacher midwives.

"Modern Trends in Gynecology and Obstetrics—Special Sessions, Communications and Motion Pictures from the International Congress on Gynecology and Obstetrics, Geneva, 1954." Ed. R. BORTH. Pp. 912. Georg & Cie, S.A., Geneva, 1955.

THE proceedings of the 1954 International Congress in Geneva were so extensive as to necessitate their reporting in 3 separate books. The first volume contained the papers

on "Prophylaxis in Gynecology and Obstetrics", and the second dealt with the scientific exhibition of clinical and experimental research. In this third volume are presented the lectures given at the special sessions as well as most of the communications made at the scientific sessions. In addition there is a useful appendix summarizing the features of 65 medical films exhibited at the congress. The book is well printed and the illustrations are of high standard. The monolingual reader is at a disadvantage as many of the papers are in French, German or Italian without translations even of the summaries. However, abstracts of most of the papers appeared in English in *Excerpta Medica* (Amsterdam) during 1954.

There are 87 papers on the gynaecological subjects, on biological aspects of tumour growth, genital cancer, benign genital disease, endocrinology, diagnostic tests and operative techniques. The 79 papers on obstetrics relate to the physiology and pathology of pregnancy, labour, operative obstetrics, diseases of the newborn and preventive medicine in obstetrics. There is, therefore, a great diversity of subject matter, from general principles and broad aspects to technical minutiae and reports of rare cases. Of necessity there are also represented old and new, orthodoxy and heresy, revelation and platitude. Altogether this is a useful reference book of some current trends in thought and practice in obstetrics and gynaecology.

"Nursing Care of the Newly Born Infant." By W. S. Craig, in collaboration with M. F. G. Buchanan, R. J. Pugh, M. Pattulo, with a chapter on Mothercraft by Miss M. J. W. Taylor. Pp. viii+472, with 226 illustrations, 24 in colour. Messrs. E. & S. Livingstone, Ltd. 1955. Price 35*s*.

In its preface this book is said to be intended for the midwife and family doctor. It will serve the needs of the former admirably. Its scope is far wider than its title suggests. It is not only concerned with the feeding and management of the newborn infant but also with its development before and after birth, its appearance and behaviour, the maladies small and large to which it is prone, and even some of the legal and administrative matters which affect it. In addition to this interesting and valuable background of knowledge about the baby it provides the midwife with clear and detailed instructions on how to care for the normal newborn; what to do if things go wrong and when to call in the doctor. At this point, however, the doctor will turn to the book for help in vain, but it would be unfair to expect a volume of this size to deal adequately with all the many problems of newborn babies with which a doctor may be faced. Nevertheless it should deservedly find a ready market amongst doctors for whom there is no modern English medical text-book on the newborn baby available.

The many illustrations are for the most part of real value and add to the agreeable presentation of the book.

"Birth Control." By various authors. *Gynécologie pratique*, **6**, 373, 451. 1955.

The whole of this issue is devoted to the subject of Birth Control and a great deal of its significance is lost to the English reader. In France, a law, made in 1920, prohibits not only the manufacture and sale of contraceptives, but also all instruction in their use. A number of eminent personalities consider that the time is now ripe for a change in this law and one feels that the editors of this journal have made a courageous step in this direction.

The contributors include Professor Knaus and the late Lord Horder. The articles consider the social and moral problems of contraception and outline the problem of abortion in France. The writers feel that the appalling frequency of abortion, which costs at least 500,000 French lives annually, can only be reduced by full sex education including contraception instruction.

There is no description of techniques, presumably because this would infringe the present law.

REVIEW OF CURRENT LITERATURE

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PHYSIOLOGY

142. **The Content of Ribonucleic Acid (R.N.A.) in the Epithelium of the Vaginal Portion of the Cervix during the Menstrual Cycle.** (Il comportamento dell'acido ribonucleinico (RNA) nell'epitelio di rivestimento della portio durante il ciclo mestruale.)

By G. Remotti and V. Bubani. *Ann. Ostet. Ginec.*, **77**, 613–618. June, 1955. 7 figs. 8 refs.

The authors have studied, by means of special staining methods, the content of ribonucleic acid in the epithelium of the vaginal portion of the cervix during the menstrual cycle. This is particularly related to the glycoproteids and mucopolysaccharides and thus to the glycogen content of the epithelium.

It is found that there is a progressive increase in the ribonucleic acid content of the Malpighian layer of the epithelium throughout the menstrual cycle. Towards the end of the follicular phase it is also present in the stratum spinosum. The maximum content is reached at about the 23rd to 24th day; thereafter there is a rapid fall to the low level seen in the post-menstrual phase.

Josephine Barnes

143. **Some Aspects of the Chemical Nature of Human Ovarian Follicular Fluid.**

By W. H. Perloff, J. Schultz, E. J. Farris and H. Balin. *Fertil. Steril.*, **6**, 11–17. Jan.–Feb. 1955.

It was observed by the authors that the actual transit speed of spermatozoa was increased when follicular fluid was added to a specimen either *in vitro* or under cover slip. Hence they deduced the fact that this fluid was an essential part of the process of ovulation, for it would not only speed the progress of the ovum into the trumpet end of the tube, but assist the advance of the sperm cell. It may be assumed therefore that this fluid emerging from the follicle is actually passed into the tube and uterus, and possibly as far as the cervix, to serve as a source of nutriment to the sperm cells in their migration upwards. These findings are especially interesting as, apart from its hormone content, follicular fluid contains fructose and a higher albumen percentage than that of serum. Such data would suggest that if an oestrogenous cyst be seen on the surface of the ovary at the time of laparotomy, it should be emptied with a syringe and then pumped into the Fallopian tube. If this be not done, then one should look for and measure the size of any ovum present. Another confirmatory observation was that spermatozoa survived and remained actively motile in follicular fluid for more than 48 hours.

V. B. Green-Armytage

144. **Use of Serial Vaginal Smears in Detecting Time of Ovulation.**

By G. M. Riley, E. Dontas and B. Gill. *Fertil. Steril.*, **6**, 86–101. Mar.–Apr. 1955.

This technique rather than that of the basal temperature curve is becoming more and more popular, as the patient herself can readily be taught how to prepare the smear which should be examined by the gynaecologist

or pathologist for 2 or 3 consecutive months in order to be sure that ovulation is regular, or for that matter even occurring. The authors give their experience of such smears from 300 patients complaining of infertility, the majority having been prepared by the patient herself. An ovulatory smear is one that represents the most advanced stage of the follicular phase, and has typical characteristics such as clarity of background, no leucocytes, maximal concentration of cornified cells with the well-known tendency for the cells to remain discretely separated. They are of the opinion that all Infertility Clinics should instruct attending patients to bring their smears regularly for microscopic examination and report.

V. B. Green-Armytage

145. **Occult Menstrual Bleeding about the Time of Ovulation.**

By Y. M. BROMBERG. *Fertil. Steril.*, **7**, 71–79. Jan.–Feb. 1956.

This paper offers still yet another method of determining whether a patient is ovulating and is based upon the discovery of occult blood on a vaginal swab at the time of ovulation. For a long time we have all used the terms mittelblut and mittelschmerz, but this test is to reveal whether the minutest quantity of blood has been shed from the uterus as a result of ovulation. A freshly prepared mixture of 25 mg. of benzidine hydrochloride and 200 mg. of barium hydroxide is dissolved in 5 c.cm. of glacial acetic acid and kept in a dark glass bottle. A cotton tipped stick is then introduced into the vagina with a slight rotary motion. After removal, one or two drops of the benzidine solution are allowed to fall on the cotton tip. A positive reaction consists in the instantaneous appearance of a bright green colour. A weak reaction consists of a greenish blue colour. If the reaction is negative no colour appears. Positive reactions are obtainable in dilutions of more than one in eighty thousand, that is when there may be only 2 red blood cells per high power field of the microscope. The test is so sensitive for haemoglobin as to give 90 per cent success. This very large success rate has been confirmed and correlated with basal temperature charts, endometrial biopsies and controlled conceptions. There is just one point to note, and that is that the test should be done on the 15th day of a normal menstrual cycle rather than before that. It has been shown that the actual mechanism of the occult bleeding which appears most often on the 15th day is by extravasation or diapedesis from the sub-epithelial endometrial vessels.

[This simple test is a valuable addition to our knowledge.]

V. B. Green-Armytage

OBSTETRICS

146. **Obstetric-Gynecologic Eponymy—Martin Naboth and Cervical Cysts.**

By H. SPEERT. *Fertil. Steril.*, **7**, 66–70. Jan.–Feb. 1956.

There must be many like the reviewer who have wondered who was the originator of the term Naboth's Follicle. It is therefore a pleasure to read that Dr. Speert of Columbia University has unearthed the fact that it was not Martin Naboth but one Professor Guillaume Desnoues of Genoa who in 1681 first discovered and wrote about the cysts of the cervix. Although Caspar Bartholinus had just announced his discovery of the vestibular glands, it was Desnoues who thought he had at last hit upon the female analogue of the male seminal apparatus, for did not these cysts when pricked and pressed upon emit large flecks of matter, and were not the small elevations at and near the mouth of the womb possessed of small openings about the size and shape of those at the verumontanum in man? Twenty-six years later in 1707 Martin Naboth in his *Treatise on Sterility in Women* acknowledges the discovery of Desnoues, but in attempting to correct the latter's views he himself erred in regarding the cervical cysts as eggs or ovisacs. Martin Naboth was born in 1675 in Germany and was in addition to being an anatomist, a Professor of Chemistry in Leipzig at the time when he wrote *De Sterilitate Mulierum*.

V. B. Green-Armytage

PREGNANCY

147. **Nutrition Studies of Pregnant Australian Women.**

By J. M. WOODHILL, A. S. VAN DEN BERG, B. S. BURKE and F. J. STARE. *Amer. J. Obstet. Gynec.*, **70**, 987–1003. Nov. 1955. 3 figs. 9 tables. 36 refs.

This study is concerned with 186 women (52 primiparae, 134 multiparae). For evaluating the diets a 5-point rating scale was used—"excellent", "good", "fair", "poor" and "very poor". The diet before pregnancy, that in the first and second halves of pregnancy, and the "over all" diets were separately assessed, and the levels of consumption of protein, calcium, vitamin B_1 and vitamin C, "the nutrients most likely to be inadequate in the average Australian diet", were used for the ratings. The toxaemia and the prematurity data were taken from hospital records.

The incidence of toxaemia was significantly different in the 5 groups. Amongst the "very poor" it was 42 per cent; in the "poor" group it was 21 per cent, in the "fair" group 9·7 per cent, 7 per cent in the "good" and 5·6 per cent in the "excellent" group. Toxaemia was more frequent in women who were overweight before pregnancy than in others—25·8 per cent and 11·8 per cent respectively.

A statistically significant relationship was also found between diet and prematurity. In the "very poor" group the incidence was 19 per cent, in the "poor" group 9 per cent, in the "fair" group 4 per cent, and in the "good" and "excellent" groups combined nil. There was, too, a consistent positive correlation between the duration of lactation and the diet before and during pregnancy.

F. J. Browne

148. **The Vitamin B_6 Requirements for Normal Pregnancy.**

By E. W. PAGE. *West. J. Surg. Obstet. Gynec.*, **64**, 96–101. Feb. 1956. 22 refs.

Vitamin B_6 is composed of pyridoxine, pyridoxal and pyridoxamine, all of which are characterized by some action on amino-acid metabolism. Experimental deficiency in humans produces a seborrhoeic dermatitis of the face and scalp, glossitis and stomatitis, weight loss, anorexia and weakness, an increased susceptibility to infections (especially urinary) and a peripheral neuritis. In infants convulsions occur. The estimated daily requirement for the non-pregnant adult is 2–3 mg. and it appears that the average American diet supplies 1·25 mg. daily. Subclinical deficiencies can be detected by biochemical tests and various workers have shown that 5 mg. daily are required by the pregnant woman. The author, in the University of California, sought evidence of this deficiency with equivocal results. He was able to show, however, that administration of pyridoxine had no effect on the incidence of pre-eclampsia. He concludes that it may be a good thing to supply 5 mg. daily to pregnant women.

D. C. A. Bevis

149. **Bonamine: An Effective New Therapy in Nausea and Vomiting of Pregnancy.**

By T. B. Lebherz and J. H. Harris. *Obstet. Gynec.*, **6**, 606–609. Dec. 1955. 7 refs.

Bonamine, a new type of antihistamine with 3 benzylic rings, is claimed by the authors to be very effective in treating nausea and vomiting of pregnancy. Of 92 cases treated, 81 per cent had excellent relief and 9·7 per cent had partial relief. Eleven of the patients were treated by intravenous therapy with good results. Side effects were conspicuous by their rarity.

The following oral dosage was found effective: 25 mg. at bedtime and 12·5 mg. at noon for 20 days.

J. G. Dumoulin

150. **Hemodynamic Effects and Clinical Application of a Mixture of Veratrum and Rauwolfia Alkaloids.**

By J. Voskian, N. S. Assali and L. Noll. *Surg. Gynec. Obstet.*, **102**, 37–44. Jan. 1956. 4 figs. 5 refs.

This paper describes a study of (I) the hypotensive effects of veratrum alkaloids and the rauwolfia alkaloid (reserpine) administered separately, and in combination, to the same group of individuals, (II) the haemodynamic properties of a mixture of the veratrum alkaloid (cryptenamine) and reserpine and (III) the clinical application of this mixture.

Part I of the study was carried out on 7 patients with pre-eclampsia. The average of the three lowest readings of blood pressure and pulse rate recorded within the first hour after injection was taken as the response to the drug.

Intravenous injection of 0·1 mg. of veratrum alkaloids resulted in an average fall of 10 per cent systolic and 14 per cent diastolic blood pressure. Pulse rate decreased by about 10 per cent. Intravenous injection of 0·2 mg. produced an average of 21 per cent of fall in systolic and of 25 per cent in diastolic blood pressure. The average fall in pulse rate was 27 per cent. The changes in blood pressure and pulse rate occurred 5–10 minutes after the injection and lasted for 45–60 minutes. They were accompanied by the usual veratrum side effects, which were more severe when the larger dose was used. There was no significant difference between the action of the various veratrum preparations.

Intravenous injection of 2·5 mg. of reserpine evoked an average fall of 8 per cent systolic and 13 per cent diastolic blood pressure. The pulse rate remained unchanged. Intravenous administration of 5 mg. of reserpine resulted in an average decrease of 22 per cent in the systolic and 28 per cent in the diastolic blood pressure. The decrease in pulse rate averaged 5 per cent. These effects became evident 45–60 minutes after the injection of the drug and lasted for periods varying from 4–12 hours. They were followed by the usual nasal and conjunctival congestion, somnolence and, in one instance, severe headache.

Administration of a mixture of 0·1 mg. of veratrum and 2·5 mg. of reserpine evoked a fall averaging 38 per cent in systolic and 40 per cent in diastolic blood pressure. The fall in pulse rate averaged 35 per cent. The changes in blood pressure and pulse rate occurred within 5–15 minutes of the injection of the mixture and lasted for periods varying from 6–24 hours. They were accompanied by very mild somnolence, nasal congestion and nausea.

The haemodynamic effects of a mixture of veratrum alkaloids and reserpine were studied in 10 patients with pre-eclampsia, 3 with essential hypertension and 2 normotensive subjects. The cardiac output showed insignificant changes but the total peripheral resistance was significantly reduced in all patients studied. Following injection of the mixture of drugs there was an initial fall in renal plasma flow (para-aminohippurate clearance) and glomerular filtration rate (inulin clearance), but this was followed by a progressive rise in both, despite the fact that the blood pressure and pulse rate were still below control values. Total renal vascular resistance decreased progressively in all cases after the injection of the drugs.

The clinical application of the mixture was investigated by employing it as the main therapeutic agent in the treatment of 22 pre-eclamptic and 4 eclamptic patients. Two of the eclamptics were treated for periods of several weeks and both were delivered of living children. The other 2 were treated for only short periods and 1 child was stillborn. In the acute phase of the disease the mixture was given intravenously as often as was necessary to keep the blood pressure close to 140/90 mm. Hg. The number of injections given to each patient varied from 2 to 6 and the interval between subsequent injections was never less than 6 hours. After the acute phase had subsided and the eclamptic patients became conscious, the mixture was given intramuscularly every 8 to 24 hours.

The pre-eclamptic patients received 1 to 2 intravenous injections during the first 24 to 36 hours and thereafter were switched to intramuscular injections. In some cases this route was continued for another 4 to 5 days and thereafter was replaced by oral therapy until viability was reached. Of the 22 patients, 18 had living babies and 4 stillborn.

The authors conclude that the long action of the mixture and the ease of its administration make it a good adjunct to the armamentarium of anti-hypertensive drugs since it simplifies considerably the treatment of acute toxaemia and diminishes the necessity for frequent injections or intravenous drip infusion. Furthermore there is no danger of sudden or precipitous fall in blood pressure since the fall is smooth and progressive, even though it occurs 5 to 10 minutes after injection.

John P. Erskine

151. **Bleeding in Late Pregnancy.**

By J. T. Louw. *S. Afr. med. J.*, **30**, 231–235. 1956. 1 fig. 6 tables. 30 refs.

The author mentions all the modern aids which have made safe the expectant treatment of placenta praevia. An aggravating problem however, is hospital overcrowding, and without extra facilities this may lead to inferior work.

After enumerating the local conditions, the 2 main causes, placenta praevia and accidental haemorrhage, are discussed. It is stressed that with adequate antenatal supervision placenta praevia should be diagnosed before bleeding occurs in many cases. The classical abdominal findings are mentioned, as is the danger of vaginal examination, unless performed with full preparation for Caesarean section. In doubtful cases placentography, which has reached a degree of 98–99 per cent accuracy is invaluable. It also relieves much needed hospital accommodation.

With regard to treatment, in 224 cases of placenta praevia, Caesarean section was performed in 142 (63·4 per cent) with a stillbirth rate of 14 (9·8 per cent). Any form of placental compression by the foetus must necessarily impair foetal oxygen supply and increase the stillbirth rate. The importance of accurately gauging foetal distress after rupture of the membranes cannot be overstressed. A posteriorly situated placenta will decrease the true conjugate. Caesarean section performed when the placenta is anterior may result in foetal anaemia. In the past 12 years in the Cape Town series 12 of the 13 patients who died as a result of placenta praevia were non-booked—the importance of antenatal supervision is obvious.

The various grades of accidental haemorrhage are discussed as are the important factors to be observed in the management. Fibrinogenopenia should be excluded. With regard to the controversy as to whether or not the membranes should be ruptured, the author favours early rupture, to remove the liquor with its high thromboplastin content and to hasten the termination of the pregnancy. Caesarean section may be necessary in the few cases which deteriorate. In 44 cases treated by rupture of the membranes or Caesarean section no mothers were lost. In 255 patients treated conservatively 8 mothers were lost—3 from haemorrhage and 5 from renal causes. The importance of antenatal supervision is shown by the loss of one mother in 49 booked cases and 7 mothers in 107 emergencies. The stillbirth rates were respectively 53 per cent and 67 per cent.

L. J. Abramowitz

152. **Treatment of Threatened Abortion with Diethylstilbestrol.**

By C. L. Liggett. *West. J. Surg. Obstet. Gynec.*, **64**, 16–21. Jan. 1956. 31 refs.

The author reviews the literature on the use of oestrogens and progesterone in the early and late complications of pregnancy and reports the case histories of 5 patients who suffered from threatened abortions. Patients who were considered infertile were given micronized diethylstilboestrol 25 mg. four times daily; this was continued for 2 months when the dosage was reduced to 25 mg. twice daily. Patients showing definite signs of threatened abortion had their dosage increased to 300–400 mg. and sometimes 500 mg. a day. The author concludes that this use of stilboestrol was mainly responsible for carrying the patients to term.

[The information given by the author about his cases would seem to indicate that other factors than the administration of oestrogen helped considerably in the successful conclusion of these 5 cases.]

D. C. A. Bevis

153. **Hyperadrenalism and Habitual Abortion.** (Hyperandrogénie et avortement habituel.)

By F. Richard. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 439–448. 1955. 4 figs. 9 refs.

This is a report of a case of hirsutism treated with cortisone throughout pregnancy, and resulting in delivery at term, after four previous pregnancies had ended in abortion.

The patient showed an abnormal excretion of 17-ketosteroids and corticoids in the urine, hypoprothrombinaemia, decreased capillary resistance, and overaction of the thyroid gland. Theories of the aetiology of the condition are discussed.

Throughout pregnancy the excretion of 17-ketosteroids, corticoids and pregnandiol, the changes in the vaginal smears, and the clinical signs were observed.

The mechanism of cortisone action, and the maternal and foetal risk of administering cortisone throughout pregnancy are discussed. *From the Author's Summary*

154. **Hormonal Imbalance in Pregnancy and Cytological Smears.** (Grossesses hypohormonales et frottis cytolytiques.)

By M. Gaudefroy. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 469–474. 1955.

The prevailing opinion is that normal vaginal smears during pregnancy imply a normal hormone balance. The author cites 14 reports of pregnancies with previous spontaneous abortion or threatened miscarriage in which the vaginal smears were normal but hormone tests showed important insufficiencies. The author does not consider that normal smears prove that there is a normal hormone balance.

From the Author's Summary

155. **Placental Inefficiency: Cervical Mucus Arborization as Aid to Diagnosis.**

By B. Zondek, I. Forman and K. L. Cooper. *Fertil. Steril.*, **6**, 523–533. Nov.–Dec. 1955.

This paper raises many points of importance and perhaps introduces matter for future research in out-patient departments. The cervical fern crystallization phenomenon [which for the sake of brevity is denoted in all American literature as the PL. Test in reference to its palm-like appearance] has been known for the last 10 years. In 90 per cent of cases it is constant from the 8th to 22nd day of the cycle in the non-pregnant patient who is normally ovulating, but it has now been shown that with normal intra-uterine pregnancy the PL. reaction is inhibited immediately after conception because the normal influence of oestrogen on the cervical mucus is now opposed by great progesterone activity. It has been estimated that 12–15 mg. of progesterone will inhibit the action of 1 mg. of oestrone in the production of normal arborization of cervical mucus. The importance of this test will be quickly realized when it is stated that out of 226 patients studied during the first trimester, 200 gave completely negative tests and 26 only slightly positive and 15 of these pregnancies terminated in abortion, and 2 were ectopics. These figures demonstrate that a positive PL. reaction in early pregnancy denotes disturbed function of the placenta and therefore should warn the clinician of the likelihood of early abortion or tubal mole formation—a fact that has been proved correct by Randall, Koff and Tusky in 97 per cent of 335 patients studied. These facts suggest that the smear or PL. test, a very simple procedure, should be done routinely in hospital clinics.

V. B. Green-Armytage

156. **Porphyria in Pregnancy.**

By J. B. Durst and M. A. Krembs. *J. Amer. med. Ass.*, **160**, 165–168. Jan. 21, 1956. 13 refs.

Porphyria is a metabolic disorder manifested by a marked overproduction of uroporphyrin and related substances. Psychotic behaviour is common in this condition and the authors describe four cases associated with pregnancy, in which the passing of red urine provided the essential clue to the diagnosis of the associated abdominal pain. There is no evidence that pregnancy causes an exacerbation in latent cases of porphyria. In 3 of the cases reviewed there were marked symptoms in the first trimester with improvement during the remainder of their pregnancies. One patient had relief only after delivery.

The aetiology of porphyria is uncertain but barbiturates are a possible precipitating cause. Lesions have been found at autopsy in the sympathetic ganglia in patients with porphyria and spasmodic contractions of the intestine have been attributed to these lesions. Symptomatic treatment of one case in pregnancy with tetraethylammonium chloride gave encouraging results.

D. W. James

157. **Malignant Osteoclastoma during Pregnancy.** (Contibuto alla conoscenza dell'osteoclastoma maligno in gravidenza.)

By F. Marazzini. *Ann. Ostet. Ginec.*, **77**, 559–584. June, 1955. 10 figs. 80 refs.

This is a long and detailed account of a case of malignant osteoclastoma occurring in a pregnant woman. The disease caused marked scoliosis and pelvic deformity and in the later stages of pregnancy, grave respiratory difficulty occurred due to the excessive curvature of the dorsal spine. A living healthy infant was delivered by Porro Caesarean section with bilateral salpingo-oöphorectomy. The mother survived the operation by 13 months, and then died of pulmonary metastases.

Josephine Barnes

158. **The Management of the Rh-Negative Mother in General Practice.**

By G. M. Bourke. *Med. J. Aust.*, **2**, 1095–1097. Dec. 31, 1955. 4 refs.

As Paediatric Registrar, the author is responsible for the admission of Rh-negative mothers and their babies from general practices to The Women's Hospital (Crown Street), Sydney. He considers that the management prior to admission could be improved.

A good history taken by the practitioner at the first visit is essential. The blood group and Rh status should be determined by the 16th week. If the patient is Rh negative the serum should be tested for anti Rh agglutinins at the 16th and the 34th week. Often it is found that a patient admitted as an "emergency" has not had the blood group determined.

In general practice the great importance of the first baby to an Rh-negative mother is not always recognized.

Babies who have developed signs suspicious of haemolytic disease of the newborn within twenty-four hours of birth, are sent to the hospital too late to achieve the best results from exchange transfusion. The baby is best brought to the hospital *in utero* rather than by ambulance after birth and often after signs of haemolytic disease are present. Rh-negative women with agglutinins should be confined in a fully equipped obstetrical hospital. This allows consultation between the obstetrician and paediatrician and for expert clinical examination and laboratory investigation. For success with exchange transfusion a skilled and experienced medical and nursing staff is necessary.

The mortality from haemolytic disease of the newborn is much greater in those babies admitted to hospital for treatment after birth than those born in a hospital where proper facilities for examination, investigation and treatment are immediately available. The decision to confine the Rh-negative woman in other than a large obstetrical hospital is an indication of defective antenatal care.

S. Devenish Meares

159. **Pregnancy After Conservative Surgery for Endometriosis.**

By G. E. Norwood. *Fertil. Steril.*, **6**, 51–60. Jan.–Feb. 1955.

This is an optimistic article dealing with 54 patients studied over a period of 15 years—indeed so optimistic that one wonders why laparotomy was done for symptomless infertility. Dr. Norwood divides the degree of involvement of the pelvis by endometriosis into 5 grades. Subsequent to conservative surgery 51 patients became pregnant out of 54, and during the actual period of analysis there were 32 abortions, and 7 premature and

54 full-term infants were born. Provided that symptomatic relief can be assured and that the skill of the conservative surgery was adequate, the author considers that the location and extent of the disease does not affect the outlook for subsequent pregnancy. The average date of conception after operation was 2 years and 2 months. He advocates that the round ligaments should be shortened, and if need be, prelumbar sympathectomy done at the time of laparotomy.

V. B. Green-Armytage

160. **Report of Pregnancies in Infertile Couples.**

By W. C. KEETTEL, R. C. BUNGE, J. T. BRADBURY and W. O. NELSON. *J. Amer. med. Ass.*, **160**, 102–105. Jan. 14, 1956. 6 refs.

The authors review the actual pregnancies accomplished in 185 infertile couples investigated at the Department of Obstetrics and Gynecology, University of Iowa. It was essentially a combined approach, and complete physical examination of both partners was carried out before laboratory procedures. In the female, tubal insufflation, a radiogram of the chest, urinalysis, blood count, estimation of protein-bound iodine and serological studies were performed at the first visit. At the second visit, two days before the anticipated menstrual period, an endometrial biopsy was done and the basal temperature graph was interpreted. In the male, the semen examination determined the pH, volume, liquefaction time, viability count, number of abnormal forms and the type of motility.

In the female the most frequent findings were menstrual irregularity and endometriosis. A high percentage of women had patent tubes, normal basal temperature graphs and secretory endometrium. In the male poor quality semen was relatively common and azoospermia was found in more than an eighth of the cases studied. The therapeutic procedures preceding pregnancy were tabulated, and it is of interest that in only 9 cases was surgery recommended. Treatment of the male was not encouraging and consisted of testosterone rebound and the use of amylase in a cervical cap in selected cases. In this series of 185 couples 58 eventually became pregnant, but 20 of these conceived through therapeutic donor insemination. In the remaining 38 patients it was difficult to assess the value of any particular form of treatment. Time and chance play an important part but the authors consider that "therapy" was a factor contributing to success in 50 per cent.

D. W. James

161. **Acute Renal Shutdown: Report of a Case Treated by Intravenous Fluids, Exchange Blood Transfusion and Peritoneal Dialysis.**

By A. N. TURNBULL. *N.Z. med. J.*, **54**, 647–650. Dec. 1955. 1 fig. 7 refs.

This report of a case of renal shutdown following an attempt by the patient to procure her own abortion by intra-uterine douching is of interest because she was admitted to hospital fifteen days after the interference, and nine days after she stopped passing urine. She had been jaundiced for a few days but this had disappeared, and she was admitted gravely ill, in an acidotic state. Haemoglobin was 5·5 g., blood non-protein nitrogen 328 mg., serum potassium 7·6 m.Eq./litre, phosphorus 16·0 mg./100 ml. and plasma bicarbonate 6·1 m.Eq./litre.

On the day of admission, blood transfusion was undertaken, and the next day an exchange transfusion was given. On the third day, a peritoneal dialysis lowered the non-protein nitrogen from 320 mg. to 170 mg. On that day urinary output began to increase and two days later diuresis was profuse. The patient gradually recovered, the blood non-protein nitrogen taking thirty-five days to return to normal.

L. Woodrow Cox.

162. **Acute Renal Insufficiency in Obstetrics.**

By E. J. SLOWINSKI. *Obstet. Gynec.*, **7**, 2–9. Jan. 1956. 19 refs.

Obstetrics is one of the chief sources of cases of acute renal insufficiency. Aetiological factors can be divided into three groups: Group 1 includes cases of peripheral circulatory failure, Group 2 incompatible transfusion and haemolytic drug reactions, and Group 3 nephrotoxic agents such as sulphonamide and quinine sensitivity, mercurial abortifacients and other poisons, septicaemia and possibly severe toxaemia.

The clinical course starts with an oliguric phase associated with haematuria, proteinuria and decreased specific gravity of the urine. After some days, lethargy, nausea, vomiting and diarrhoea may ensue, followed by uraemic coma and death. The major cause of death is cardiac failure, accelerated by over-hydration.

In the past 4 years 36 patients with acute renal failure have been treated at Georgetown University Hospital, Washington, by means of the artificial kidney. Ten of these were associated with pregnancy. The Kolff-Merrill type of kidney was used. Blood was led from the radial artery through a length of cellophane tubing wound spirally around a drum. The tubing is passed through a rinsing fluid maintained at 100° F. in a 100-litre container. The dialysing solution is changed as necessary to reduce individual solutes or water in the patient's blood, which is then returned to a vein in the forearm. The problems in the management of the artificial kidney are multiple and can be handled only by experts.

Post-partum the involuting myometrium is a source of potassium, so that particular effort must be made to reduce the potassium load. Blood replacement should be made with fresh blood. Glucose infusions with adequate insulin coverage are important, as are adequate correction of acidosis and of calcium and phosphorus abnormalities. Cation exchange resins administered by mouth or retention enema help to reduce the plasma potassium. As important as any other measure is the maintenance of adequate fluid balance and the prevention of over-hydration.

J. G. Dumoulin

163. **The Changing Aspects of Pneumonia Complicating Pregnancy.**

By H. OXORN. *Amer. J. Obstet. Gynec.*, **70**, 1057–1063. Nov. 1955. 12 tables. 13 refs.

The main interest of this paper, which is based on 64

cases treated in the Royal Victoria Hospital, Montreal, from 1926 to the end of 1953, is the comparison of data from the pre- and post-antibiotic eras—35 from the former and 29 from the latter. The paper is of special interest as, with one exception in a Dutch journal in 1954, it is the only one published on pneumonia in pregnancy since the introduction of penicillin in 1941 or even of the sulpha drugs in 1936.

It was found that antibiotics made no material difference in the incidence of premature interruption of pregnancy in pneumonia, which was over 50 per cent. The maternal mortality was however reduced from 20·0 per cent to 3·5 per cent, and the foetal loss when the duration of pregnancy had been 37 to 40 weeks fell from 19 per cent to nil.

Treatment should be directed towards the pneumonia without active obstetrical interference, and induction of labour is contra-indicated. In fact, the only obstetrical interference permissible is the performance of elective low forceps delivery to relieve the embarrassed pulmonary and circulatory systems of the added strain of the downbearing efforts. The anaesthetic of choice is local infiltration. Oxygen may still be used with advantage during labour and given in sufficient concentration to prevent cyanosis.

F. J. Browne

164. **Infectious Hepatitis Complicating Pregnancy.**
By K. B. Rao and M. N. Ganapathy. *J. Obstet. Gynaec. India*, **6**, 210–215. Dec. 1955. 4 figs. 14 refs.

An outbreak of infective hepatitis is described, in which 28 cases occurred in pregnancy and the puerperium. The highest incidence was in the third trimester, only 2 cases occurring after delivery. During the same period, 38 cases occurred in the same area in non-pregnant women.

The main symptoms were of anorexia, vomiting, epigastric pain, and fever, with jaundice lasting from 3 weeks to a month. Eight cases became comatose, of which only one recovered. Treatment was by hospitalization, and a high carbohydrate, high protein, and low fat diet, supplemented by protein hydrolysates. In addition, patients got dextrose, calcium gluconate, and vitamin C, with methionine intravenously, and vitamin K intramuscularly. Some of the comatose patients were given aureomycin through a Ryle's tube, but without success. Obstetric treatment was conservative in all cases.

Of the 38 non-pregnant women, 2 died. Of the 28 maternity cases, 8 died in the third trimester, and there was one post-partum death. Post-mortem examination, when done, showed diffuse acute liver necrosis.

Fourteen deliveries were premature. Post-partum haemorrhage occurred in 9 patients, 4 of whom required a blood transfusion.

Of the 20 babies born to the 19 mothers who lived, there were 3 stillbirths, and 2 neonatal deaths. None of the infants showed evidence of jaundice.

J. McKiddie

165. **Passive Protection Against Rubella.**
By H. Ward and G. Parker. *Med. J. Aust.*, **1**, 81–83. Jan. 21, 1956. 1 table. 3 refs.

A statistically sound study of the degree of passive immunity conferred by the injection of convalescent serum shortly after exposure to rubella has been made by the New South Wales Red Cross Blood Transfusion Service. A single intravenous injection of 30 millilitres of serum obtained from adult volunteers who gave a donation of blood approximately 3 weeks after the disappearance of the rubella rash was used. Over the past four years this serum has been made available to any doctor who applied, provided that (1) the patient was not more than 16 weeks pregnant, (2) the exposure was direct and (3) the serum could be injected not more than 5 days after direct exposure to rubella infection.

During the last year the results have been studied and compared with an untreated control group. There were 541 passively immunized and 152 in the control group. One per cent of the subjects in the treated group subsequently contracted the disease compared with 11 per cent in the control group. The authors conclude that a dose of 30 millilitres of convalescent serum is effective in protecting pregnant women exposed to rubella infection.

S. Devenish Meares

166. **New Sign in Roentgen Diagnosis of Advanced Ectopic Pregnancy.**
By A. Weinberg and A. S. Sherwin. *Obstet. Gynec.*, **7**, 99–101. Jan. 1956.

The new sign in the X-ray diagnosis of advanced extrauterine pregnancy which the authors introduce is the appearance of foetal parts posterior to the lumbar spine of the mother in a true lateral projection.

Other signs which may be recognized are an eccentric position of the foetus, malposition, lack of visualization of the uterine wall, unusual clarity of foetal parts and maternal intestinal gas shadows overlying the foetus.

J. G. Dumoulin

LABOUR

167. **Primigravid Labor: A Graphicostatistical Analysis.**
By E. A. Friedman. *Obstet. Gynec.*, **6**, 567–589. Dec. 1955. 15 figs. 91 refs.

A statistical analysis of the rate of cervical dilatation is presented by the author from Columbia University and Medical Centre. Cervical dilatation in centimetres was plotted graphically against time in hours in 500 primigravidae. Labour terminated spontaneously in 40·4 per cent, by forceps in 55 per cent and by Caesarean section in 1·8 per cent. There were 2·8 per cent breech deliveries and 0·86 twin births.

The sigmoid curve obtained showed a latent phase for the first 8½ hours of labour, followed by an active phase of 6 hours when the rate of dilatation speeded up, terminating in full dilatation. The active phase was subdivided into 3 components, the middle one showing the most rapid change: it is preceded and followed by acceleration and deceleration components.

Statistical analysis showed the upper limit of normal for the latent phase as 20½ hours and for the active phase as 15 hours. The maximum duration of a normal first stage was 28½ hours, and the second stage 2½ hours.

The latent phase was found to be prolonged when the cervix was "unripe", when heavy medication was used, and in primary uterine inertia. Inertia in the active phase was associated with excessive sedation and/or foeto-pelvic disproportion, and primary uterine inertia might continue in this phase. The graph in precipitate labour showed a normal first phase, but foreshortening of the active and deceleration phases. Prolongation of the deceleration phase was noted in inertia and disproportion: caudal anaesthesia and occipito-posterior positions were also found in this group.

In studying the effect of excessive sedation on labour, the author showed that the latent phase is markedly prolonged and the active phase to a lesser extent. Pethidine and scopolamine were the drugs used. He showed that caudal anaesthesia should be limited to uncomplicated labours, should not be started until the active phase and should not be preceded by excessive premedication.

Pitocin was shown to be effective for inducing labour electively and a powerful agent for combating inertia. It stimulates labour in moderate degrees of disproportion, but its value in cases of disproportion is a two-edged sword. Disproportion was associated with slower cervical dilatation in the active phase, particularly in deceleration, and it accounted for all cases of secondary uterine inertia. Labours with associated posterior positions were normal, except for a slight prolongation of deceleration. Psychological preparation for childbirth was considered to shorten the latent and active phases of cervical dilatation. In cases where the membranes ruptured during the latent phase, this phase seemed to be slightly lengthened. Maternal age did not seem to alter the rate of dilatation.

Finally, the author states that in spite of statistical evidence many of the conclusions he reaches are on tenuous ground.

J. G. Dumoulin

168. **One Hundred Perfusions of Posterior Pituitary Extract.** (Cent perfusions d'extrait post-hypophysaire.)
By J. Hannes. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 489–503. 1955. 10 tables.

For induction of labour perfusion was successful in 85 per cent of cases at term, and 64 per cent before term. The success rate if a second induction has been given and followed by a surgical induction has been 93 per cent at term, and 85 per cent before term. For stimulation of uterine action in cases of inertia the method has been successful in 95·5 per cent of patients.

The solution employed is usually 9 units of orasthin per litre. A total dose of 3 units or less has been sufficient in 54 per cent of the cases. The average duration of labour was 7½ hours for the primiparae, and 4 hours and 20 minutes for the multiparae. The perfusion should be continued until after the third stage of labour. It is absolutely safe for mother and child.

From the Author's Summary

169. **A Study of the Vasopressor Effects of Oxytocics When Used Intravenously in the Third Stage of Labor.**
By L. B. McGinty. *West. J. Surg. Obstet. Gynec.*, **64**, 22–28. Jan. 1956. 17 refs. 8 tables.

The author confines his study to the effects of commonly used oxytocics on the blood pressure. Two hundred patients were divided into four equal groups. One group received 0·2 mg. of methergine intravenously, the second group was given 0·2 mg. of ergonovine i.v., the third group received 5 units of pitocin i.v. and 5 units i.m., while the control group received 1 ml. of normal saline i.v. All patients had normal deliveries under pethidine and scopolamine analgesia and pudendal block anaesthesia, the local anaesthetic containing a certain amount of adrenaline. The blood pressure on admission was used as a base line, and the blood pressure was taken at intervals of 5, 15 and 60 minutes after the drugs were given. The results indicate that methergine and ergonovine have equal vasopressor effects, although the author thinks that methergine is perhaps the better drug in the already hypertensive patient. Pitocin, although purified, still shows more severe vasopressor effects than the ergot derivatives. These drug effects usually resolve within one hour and can thus be distinguished from toxaemias. It was noted that in the control group using saline injections, the amount of post-partum bleeding was greatly increased.

[There does not seem to be much to choose between any of the drugs used as the author draws his conclusions from very small differences between the different groups.]

D. C. A. Bevis

170. **Prolonged Labor.**
By W. C. Keettel and G. S. Prettis. *Obstet. Gynec.*, **7**, 15–22. Jan. 1956. 13 refs.

The authors found that the incidence of labour lasting 30 hours or over was 3·2 per cent, and they report on 891 prolonged labours. They show that induction of labour is not associated with a high incidence of prolonged labour, but foetal position and minor degrees of disproportion are. It is difficult to assess whether abnormal foetal positions, such as posterior and transverse positions of the occiput, are the cause or the result of prolonged labour.

Since 1950 labour has not been permitted to go beyond 40 hours unless definite progress is being made. Since 1945 Dührssen's incisions and manual dilatation of the cervix have been used. In the series 238 patients (26·6 per cent) had a second stage lasting over 2 hours. The frequency of serious post-partum haemorrhage was high, 87 patients (9·8 per cent) having a loss of 600 ml. or more. There were 154 cases (17·3 per cent) with intra-partum fever, and 180 (20·2 per cent) with 2 or more days of fever, chiefly due to endometritis. Maternal mortality was 0·45 per cent (4 cases), the last occurring in 1941. The perinatal mortality was high, being 11·2 per cent. Twenty-one of the neonatal deaths were due to intracranial haemorrhage.

The only effective methods of stimulating contractions were rupture of the membranes and intravenous pitocin. Large doses of oestrogens, enemas and calcium gluconate were useless. However, intramuscular pitocin was of limited value and intravenous pitocin was not as successful as some authors have suggested.

In recent years more patients were delivered by

Caesarean section with improvement in the foetal survival rate. The extra-peritoneal type of operation was used. It was indicated when the patient had failed to respond to pitocin and when the total length of labour was nearing 40 hours. With this type of management the perinatal mortality should not exceed 4 per cent.

J. G. Dumoulin

171. **The Aetiology of Post-partum Haemorrhage.**

By C. H. DE BOER. *Brit. med. J.*, **2**, 1187–1189. Nov. 12, 1955. 2 refs.

Four hundred and five cases out of 2,444 successive vaginal deliveries at the London Hospital during the years 1950–52 were complicated by post-partum haemorrhage —an incidence of 16·5 per cent. In the years under review it was not the practice to administer ergometrine before delivery of the placenta.

Prolonged labour, operative delivery and anaesthesia were found to be the main aetiological factors in the production of post-partum haemorrhage. These three factors were not infrequently associated in individual cases.

Over-distension of the uterus, accidental haemorrhage and placenta praevia, often quoted as being aetiological factors, were found not to be so in this series. Of the 405 patients who bled excessively the primigravida-multipara ratio was 3:2 which is the same as the admission ratio to the Unit. Though fibroids were diagnosed on a number of occasions only in one case was post-partum haemorrhage thought to be caused by the tumours—this case, a submucous fibroid. No case of a fibrinogenaemia was diagnosed.

Manual removal of the placenta was performed because of haemorrhage in 48 cases.

Follow up of a number of patients in the series confirmed the fact that post-partum haemorrhage is apt to recur in subsequent pregnancies, and hospital confinement is recommended for all patients giving a previous history of this complication.

R. W. Grayburn

172. **Annular Detachment of the Cervix.**

By F. G. GRANT. *Brit. med. J.*, **2**, 1539–1540. Dec. 24, 1955. 7 refs.

Annular detachment of the cervix is an uncommon complication of labour. The occurrence was originally thought to be associated with cephalo-pelvic disproportion but in more recent years it has come to be recognized as a late result of cervical dystocia. Three associated features are enumerated: (1) Strong uterine contractions. (2) Foetal head low in the pelvis. (3) A thin well-effaced cervix with an external os surrounded by a rim of hard fibrous tissue and poorly dilated for the length of time the patient has been in labour.

Detachment is due to devitalization by pressure of the foetal head on the unyielding cervix. A great proportion of patients are primigravidae. The condition may be prevented by early recognition and treatment by digital dilatation, cervicotomy or Caesarean section. Perusal of the literature reveals that the maternal mortality rate is 7–11 per cent and stillbirth rate 29–40 per cent. Infection is the danger to the mother. Haemorrhage is not a feature of the complication.

A case is reported in which the above features were present and the cervix became detached. The patient, a primigravida aged 26, came into labour spontaneously at the 41st week of pregnancy. She had an android pelvis but there was no disproportion. Though uterine contractions were good, the cervix was very slow to dilate. After 74 hours in labour the membranes ruptured spontaneously and as rectal examination showed the cervix to be only half-dilated it was decided to effect delivery by Caesarean section. While preparations were being made, however, a living female infant weighing 7 pounds (3·2 kg.) was delivered spontaneously per vaginam. Subsequently a rim of cervix 1 inch (2·5 cm.) thick and admitting four fingers, was found to have been almost completely detached. The process was completed by ligation and excision. The puerperium was uneventful, and examination six weeks later revealed a healthy cervix almost flush with the vaginal vault. The patient became pregnant again two years later and was delivered normally of a living infant weighing 8 pounds (3·6 kg.).

R. W. Grayburn

173. **Rupture and Perforation of the Uterus in Association with Pregnancy, Labour, and the Puerperium.**

By K. FEENEY and A. BARRY. *Brit. med. J.*, **1**, 65–73. Jan. 14, 1956. 2 tables. 34 refs.

The authors, Masters of the Coombe Lying-in Hospital and the National Maternity Hospital, Dublin, review 45 cases of rupture and perforation of the uterus in association with pregnancy. The maternal mortality was 15·5 per cent. Sixteen cases were due to rupture of scars, mainly Caesarean. The risk of rupture of a scar is apparently increased by each following pregnancy and each vaginal delivery, by high parity, by multiple pregnancy, by a large foetus, by hydramnios and by implantation of the placenta over the scar. The authors stress the frequency of silent rupture in these cases. Two cases in which there was also a rupture of the bladder are described, and the authors advise against unnecessary downward dissection of the bladder in the lower segment operation.

There were two cases of rupture with shoulder presentation. The speed with which rupture may occur in these patients is stressed. If the uterine artery has been torn and retracted, the surgeon is recommended to tie instead the internal iliac artery on that side. Eleven cases followed obstetric operations, including internal version, forceps deliveries, manual removal of placenta, and evacuation of abortion.

Other groups include rupture due to obstruction, especially hydrocephalus and brow presentation, the administration of pituitrin, and spontaneous rupture in the grande multipara.

The authors describe four clinical groups. There is a "silent" group, with discomfort, slight bleeding and pallor, and failure of further dilatation of the cervix, even though contractions may continue. In the "common" type of rupture, pain, faintness, bleeding

and pallor gradually develop with tenderness on palpation and foetal death. Contractions usually cease but may continue with cessation of cervical dilatation. In the "violent" variety there is a sensation of something giving way, with ease of palpation of foetal parts, bleeding and rapid collapse. In a fourth group there is often delay in diagnosis after delivery, with insidious slight post-partum bleeding and gradual general deterioration.

Treatment is summarized—the authors stressing the importance of early diagnosis and blood transfusion. Occasionally the rent may be repaired with justification. Rupture of the vaginal vault extending to the broad ligament may occasionally be treated by packing, followed by close observation. *Eileen Wilson*

174. **Ruptured Uterus.**

By L. B. Voogd, H. B. Wood and D. V. Powell. *Obstet. Gynec.*, **7**, 70–77. Jan. 1956. 18 refs.

The incidence of ruptured uterus at Cleveland City Hospital over an 11-year period was 1 in 1,432 (12 ruptures in 17,181 deliveries). Two were secondary to previous Caesarean section, 8 were spontaneous due to other causes, and 2 secondary to obstetric trauma. Nine of the ruptures were complete. In the authors' clinic, classical section was restricted to cases of transverse lie, rare emergencies and a few cases associated with cornual resection. In most cases the rule "Once a section, always a section" was adhered to. During the 11-year period there were 428 sections performed with no maternal mortality.

No malpresentations contributed to rupture in the series. Symptoms and signs included anxiety and restlessness, and weakness and dizziness in 4 cases. Nine exhibited shock. Abdominal pain was present in 10, and rebound tenderness in 5. The uterus was firm and tender, and contractions were either absent or tetanic. Vaginal bleeding was found in 7 cases. The site of rupture was the anterior lower segment in 3 cases, and involved the lateral wall from tube to cervical isthmus in 7 cases. There was one rupture of a classical scar, and in the remaining case rupture occurred in the anterolateral portion of the lower segment.

There were 1 maternal and 7 foetal deaths. Ten of the surviving mothers had subtotal hysterectomy performed; one had the right horn of a bicornuate uterus removed. One patient survived without further therapy other than uterine and vaginal packing.

J. G. Dumoulin

175. **Prolapse of the Umbilical Cord. An Analysis of Eighty-five Cases at Louisville General Hospital.**

By J. Schultz. *Obstet. Gynec.*, **6**, 657–662. Dec. 1955. 11 tables. 6 refs.

At Louisville General Hospital, Kentucky, there were 85 cases of prolapsed cord in 28,494 deliveries, an incidence of 0·3 per cent. The foetal mortality rate was 40 per cent. Excluding anomalies incompatible with life and the infants adjudged dead when the prolapse was recognized, there were 69 cases with a foetal loss of 24·6 per cent.

In 52 per cent of cases, breech or transverse presentation or a "floating head" was present. In 17·4 per cent prolapse of the cord followed obstetric manipulation: 11·6 per cent were attributed to artificial rupture of the membranes. Other causes included twins, placenta praevia, disproportion and foetal anomalies. Prolapse did not seem to be more common in multiparous patients. Prematurity was present in 41 per cent of cases.

If the prolapse occurred when the cervix was less than half dilated the foetal prognosis was poor, but in the majority of cases labour was well advanced when the prolapse took place. Caesarean section offers the best chance when the cervix is not fully dilated. Version and extraction carries the highest foetal mortality. There was 1 maternal death which was thought to be due to an excessive amount of chloroform anaesthetic.

J. G. Dumoulin

ANAESTHESIA

176. **Complications of Low Spinal Anesthesia in Obstetrics.**

By C. E. Gibbs and C. L. Cooley. *West. J. Surg. Obstet. Gynec.*, **64**, 76–79. Feb. 1956. 13 refs.

The authors have previously published a review of 4,000 patients delivered under low spinal anaesthesia (Torkelson and Cooley, *West. J. Surg. Obstet. Gynec.*, 1951, **59**, 533) and now report the results in 9,127 cases delivered between 1947 and 1954. There was an increased incidence of malposition and 28 per cent of the patients required manual or forceps rotation, but the authors state that this was easy to perform and did not cause an increase in maternal or foetal damage. Fifteen per cent of patients suffered from a drop in blood pressure of 20 mm. Hg or more but no ill effects were produced. Two patients given spinal anaesthesia died, both following abruptio placenta. Ten per cent of the patients developed headache but this was severe in less than 1 per cent; the use of "cafergot" is recommended for this but spinal headache is not considered to be a major problem. Bladder atony was not very common. No neurological symptoms were found in the puerperium and 862 patients were followed up for 6–12 months but no permanent sequelae were found. The authors conclude that the technique is very satisfactory.

D. C. A. Bevis

177. **Effect of the Analgesic Nisentil on Uterine Contractions Considered by Parity, Stage of Labor, and Status of Membranes.**

By S. B. Ekelman and S. R. M. Reynolds. *Obstet. Gynec.*, **6**, 644–651. Dec. 1955. 4 figs. 5 tables. 15 refs.

The effects of a new intravenous analgesic called Nisentil were studied by the authors in 30 patients in labour whose antenatal course had been normal. The total dose used varied between 10 and 90 mg. The drug produced an immediate but variable analgesic effect. Its outstanding feature was relief of pain, so that patients were completely relaxed in a light sleep. All were delivered under pudendal block. The duration of maximal analgesia was within 1 hour, and the total duration of analgesia within 2 hours. No amnesia was produced.

A two-channel tokodynamometer was used to record uterine contractions. In most primiparous patients Nisentil caused a decrease in the intensity of uterine activity, most pronounced early in the first stage. Similarly it depressed activity in 6 of 8 multiparous women with membranes intact, although not in 3 multipara with ruptured membranes.

Newborn respiratory depression was seen in 6 cases but was slight. In no case was depression seen when 40–60 mg. of Nisentil was given 2 hours or more prior to delivery.

J. G. Dumoulin

MATERNAL MORBIDITY

178. **Late Sequelae of Unrecognized Separation of the Symphysis Pubis in Obstetrics.** (Les disjonctions obstétricales de la ceinture pelvienne méconnues et leurs conséquences tardives.)

By L. Godefroid. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 504–515. 1955. 6 figs. 14 refs.

Although separation of the pelvic girdle by obstetrical trauma is rare, spontaneous separation is more frequently seen, and occurred in 4 out of 2,000 deliveries. It often recurs, and may become chronic. The early effects are weakness of the lower limbs, and pain at the level of the symphysis with diastasis and abnormal mobility. This stage is often unrecognized.

In the chronic stage the pain is no longer found at the level of the symphysis; it becomes lumbo-sacral because of sacro-iliac strain and contraction of the extensors. The symptoms are accentuated before periods, and this may lead to diagnostic errors. Infiltration of the sacro-iliac region brings about the disappearance of all the symptoms, localizes the pain, and confirms the diagnosis. If repeated it may lead to recovery.

In stubborn cases Tavernier's transiliac arthrodesis gives good results with little risk.

From the Author's Summary

179. **Diabetes Insipidus in Association with Post-Partum Hypopituitarism.**

By T. Doxiades and M. Tiliakos. *Brit. med. J.*, **1**, 23–26. Jan. 7, 1956. 4 figs. 21 refs.

The occurrence of symptoms of diabetes insipidus in association with post-partum necrosis of the pituitary anterior lobe is exceedingly rare.

The case reported concerns a married woman aged 33 who was delivered by Caesarean section in the eighth month of pregnancy because of eclampsia. Considerable post-partum haemorrhage occurred. Breast activity was subsequently completely absent. Pubic and axillary hair disappeared within a few days, and the hair of her head and eyebrows became thin. Menstruation did not return. Four weeks after the operation diabetes insipidus ensued and lasted for about 3 years. The patient complained of weakness, sensitivity to cold and absence of sweating. She became dull and apathetic and lost interest in her home and friends. Six months later she became myxoedematous (B.M.R.—25 per cent); her features became coarse and she developed a generalized oedema. She was treated with various thyroid preparations but her condition gradually deteriorated. There was marked atrophy of the vulva, vagina and uterus. The thyroid gland was not palpable.

Laboratory investigations are enumerated. From these the authors conclude that the diagnosis was probably that of post-partum hypopituitarism with secondary myxoedema and transient diabetes insipidus. The patient was treated with D.C.A., thyranon, testosterone propionate and oestradiol. After about 6 weeks a good diuresis occurred, oedema decreased, as did the body weight, and the basal metabolic rate increased to +7 per cent. The patient became mentally alert again and her skin normal.

The authors, after discussing the problem, are unable to explain this association of diabetes insipidus with hypopituitarism but they are in no doubt that it does occur occasionally.

R. W. Grayburn

OPERATIONS

180. **The Use of the Systemic Hemostat Carbazochrome Salicylate.**

By J. C. Barcala. *West. J. Surg. Obstet. Gynec.*, **64**, 88–95. Feb. 1956. 32 refs.

Carbazochrome salicylate is derived from an oxidation product of epinephrine and is adrenochrome monosemicarbazone-sodium salicylate. It has no vasoconstrictor or vasodilator actions and is specific for conditions characterized by increased capillary permeability. It does not interfere with coagulation and may be used at the same time as coagulants and anticoagulants, but antihistamines should be discontinued for 48 hours before its administration as they tend to inhibit it.

The author reviews the effect of the drug in 330 surgical cases, 13 of which were obstetric or gynaecological. The results were satisfactory in cases where there was capillary or placental oozing.

[The dose would appear to be 5 mg. intramuscularly but the author does not mention this and the cases reported are too vague for further evaluation.]

D. C. A. Bevis

181. **Vaginal Extraperitoneal Transverse Lower Segment Section for Interruption of Pregnancy.**

By N. Ojima. *West. J. Surg. Obstet. Gynec.*, **64**, 82–87. Feb. 1956. 3 figs. 8 refs.

The author, from Tokyo University, reviews the history of vaginal operations for the termination of pregnancy in the 2nd and 3rd trimesters and describes a relatively new technique which is gaining favour in Japan (where, apparently, abortions are legal). The lower segment is almost 1 cm. long in the 4th month and is about 4 cm. from the external os. A crescent shaped transverse incision is made in the vaginal mucosa, its depth in the middle being enough to reach the uterine fascia but being shallow at its ends to avoid damage to the venous plexuses round the utero-vesical ligaments. Dissection of the bladder from the cervix is done with the finger-tip after incision of the so-called ligamentum vesico-cervicale.

A transverse incision is made in the lower segment below the white line of the utero-vesical pouch and where the uterine muscle is distinctly softer, the lower segment near the cervix is pushed backwards and fixed by another finger, and the incision enlarged by forceps and fingers. The membranes now protrude and pituitary extract is injected into the uterus to minimize bleeding. The fundus is now pushed down and before extracting the foetus the anterior and posterior cervical lips are pulled firmly down to further minimize bleeding by stretching the uterine vessels. After suturing the uterine wall and vaginal mucosa separately, no drain is put through the cervix; indeed it is best to keep the cervical canal untouched and to allow spontaneous drainage. If sterilization is indicated, the tubes may be ligated after closing the uterine incision and opening the peritoneal fold.

In 1950 the author investigated 87 fatal cases in 39,550 patients who had their pregnancies terminated, the risk of interference after the 4th month is 40 times as great as that in the 2nd–3rd month but no deaths followed the use of vaginal section. This may have been due to the fact that only skilled obstetricians perform the operation. No bladder injuries have been reported following the technique outlined.

D. C. A. Bevis

182. **The Forceps in Present-day Practice.**

By A. M. CLAYE. *N.Z. med. J.*, **54**, 634–641. Dec. 1955. 17 refs.

This paper was presented at the Biennial Conference of the N.Z. Branch of the British Medical Association by the guest speaker. It begins by reiterating the words of McClintock and Munro Kerr about the forceps, and stresses the need for gentleness in the use of the instrument. The writer proceeds to give his views on the place of episiotomy and the use of pitocin in delay in the second stage. The use of pitocin when delivery is not urgent, there is no obstruction, the occiput is anterior and the head is below the ischial spines is safe, if uterine contractions are not strong. Forceps delivery is chosen if pitocin or episiotomy fail, and if there is delay with the occiput transverse or posterior, preceding the extraction in the latter cases by rotation.

After mentioning "trial of forceps", Kielland's forceps and the use of forceps for the premature baby, the author goes on to warn readers that cases of "failed forceps" still occur due to attempted delivery before the cervix is dilated. He advises a vaginal examination by the operator, before the patient is anaesthetized, to be quite certain that the cervix is fully dilated. If immediate delivery is imperative, incision of the cervix is safe in certain conditions, otherwise Caesarean section is necessary.

The risks of anaesthesia for forceps delivery are dealt with, and the technique for using local anaesthesia is given in detail. The latter method is advised for low forceps operations.

The author concludes with another plea for gentleness in the use of forceps.

L. Woodrow Cox

183. **Caesarean Section: Its Use in Difficult Labour in Primigravidae.**

By D. BAIRD. *Brit. med. J.*, **2**, 1159–1163. Nov. 12, 1955. 7 refs.

Since the discovery of the sulphonamides and the antibiotics the incidence of Caesarean section has increased. The effect of this is discussed after a detailed examination of the relationship of Caesarean section rates and stillbirth and maternal mortality rates occurring in all first births in the City of Aberdeen between the years 1938 and 1954.

The incidence of Caesarean section in primigravidae rose from 1·10 per cent during the years 1938–42 to 3·8 per cent in the years 1951–54. During the same period of time the stillbirth rates from birth trauma and unexplained intra-uterine death fell by two-thirds and the maternal mortality rate from difficult labour was reduced by half.

The author concludes that the great improvement is in part due to the avoidance of difficult vaginal delivery by the greater use of Caesarean section. Other factors contributing to the improvement are the increased incidence of hospital confinements and the recognition and avoidance of the dangers of postmaturity.

It is apparent that in reducing the stillbirth rate a certain number of Caesarean sections may be performed unnecessarily, but the percentage of unnecessary operations could be reduced by improved selection of cases. It is important to keep the Caesarean section rate at an optional level (a rate of between 3 per cent and 5 per cent in primigravidae is suggested). For one thing, although the operative risks are small today, the total maternal deaths may be just as great with many operations carrying a low mortality as with few operations carrying a high mortality risk. And then it may be found that although there may be a decrease in the incidence of certain complications of childbirth following the greater use of Caesarean section, the incidence of other complications may rise, so affecting the advantage.

A follow-up study in Aberdeen has shown that when Caesarean section is carried out in a first pregnancy there is a deterrent or delaying effect on further pregnancies—another reason for avoiding the unnecessary Caesarean section as far as possible. A sense of balance must be maintained, and whereas it may be of primary importance to secure a living child at all costs in the case of an "elderly" primigravida, the acceptance of some slight risk may be justified in the case of a young primigravida in the interests of future fertility.

In general, in healthy well-grown young women the pelvis is normal, uterine function is good and labour easy, and in addition, placental function is good. After the age of 25 disordered uterine action is more common and placental function becomes steadily less efficient, especially if the pregnancy goes beyond 40 weeks.

R. W. Grayburn

184. **Shall We Discard Extraperitoneal Cesarean Section?**

By E. W. CARTWRIGHT. *West. J. Surg. Obstet. Gynec.*, **64**, 51–60. Feb. 1956. 56 refs.

A questionnaire on the use of this operation was sent to 476 obstetricians on the Pacific coast of America. Four hundred and forty-three replied and 304 had used the technique; 161 (55 per cent) have now abandoned the method, the majority because they thought that the transperitoneal approach with antibiotics and chemotherapy was satisfactory. The author considers this to be evidence that interest in the operation is still considerable and that this technique still has its place in the frankly infected patient; these cases are necessarily rare but the obstetrician should be prepared.

[The author uses the Physick-Sellheim technique and bases his argument on reports in the literature.]

D. C. A. Bevis

185. **Influence of Anesthesia on Infant Mortality Rate in Cesarean Sections.**

By P. C. LUND. *J. Amer. med. Ass.*, **159**, 1586–1591. Dec. 24, 1955. 10 refs.

The numerous articles in the current medical literature indicate that there is a wide divergence of opinion regarding the choice of anaesthesia for Caesarean section. Although numerous obstetric factors contribute to the foetal mortality in Caesarean section, the prime factor is the maternal complication for which the operation is performed. Second in significance is the period of gestation or the weight of the foetus. The so-called "intrinsic foetal mortality rate in Caesarean section", unless due to intracranial haemorrhage, is in the author's view actually due to the effects of anaesthesia.

An analysis of 671 consecutive Caesarean sections was made from the Department of Anaesthesiology, Conemaugh Valley Memorial Hospital. All cases in this series were performed with one of three types of anaesthesia: (1) Spinal: from 9 to 11 ml. of 0·1 per cent hypobaric tetracaine, 423 cases. (2) Epidural: 20 to 25 ml. of 2 per cent hexylcaine or xylocaine, 45 cases. (3) General: 100 mg. of thiamylal sodium followed by cyclopropane, with relaxants and an endotracheal tube after delivery of the baby, 203 cases. The technique of each method is discussed and the three types of anaesthesia are tabulated against (1) the indication for the Caesarean section; (2) the causes of foetal mortality; (3) complicated Caesarean sections with foetal mortality; and (4) foetal weight and mortality rate.

The responsibility for resuscitation in these cases belongs to the anaesthetist. The three stages requiring resuscitation are described as those of depression, spasticity, and flaccidity. In the latter stage aspiration of the main bronchi is advocated in addition to the usual tracheal aspiration. After a mathematical analysis of all the figures given the author concludes that anaesthesia has a marked influence on the perinatal mortality rate in Caesarean section.

D. W. James

INFANT

186. **The Observed Embryology of Human Single-Ovum Twins and Other Multiple Births.**

By G. W. CORNER. *Amer. J. Obstet. Gynec.*, **70**, 933–951. Nov. 1955. 16 figs. 33 refs.

In this, the annual Joseph L. Baer lecture, Corner discussed the three methods by which single ovum twins may arise, namely by division of the fertilized egg cell into two daughter cells, by duplication of the inner cell mass in one blastocyst, and by duplication of the embryonic rudiment and primitive streak after the amniotic cavity has formed.

Though the first method has not yet been observed in early human embryos it has been demonstrated experimentally in rats and rabbits, each of the two daughter cells being apparently totipotent and capable of developing into a normal foetus. The two separated ova would start their intra-uterine careers exactly as if they were double ovum twins, would be separately implanted and form each its own placenta and membranes, and the resulting twins would be identical. Only one corpus luteum would be present in the ovary.

Nevertheless the production of twins by separation of the blastomeres can never be absolutely proved by inspection of the products of conception, though genetic and obstetrical evidence favours its occurrence, for about one-third of all identical twins are enclosed in separate chorions with separate placentas and so must have come from separation of fertilized egg cells.

In the second method of development of identical twins, namely by duplication of the intermediate cell mass in one blastocyst, each will have its own amnion and yolk sac, but there will be a single chorion and placenta. A pair of twins of this type at 16 or 17 days was found in 1952 in a human uterus removed at operation and is now in the Carnegie collection. In this specimen a single chorion contains twin embryos each with its own yolk sac. Examination of the placenta and membranes after delivery reveals the doubled amnion and permits the retrospective deduction that the two infants must have come from two inner cell masses in one blastocyst.

In the third variety two embryos will appear on the floor of one amniotic cavity and will have a common yolk sac. This arrangement will persist till birth when the obstetrician will find two infants in a single chorio-amniotic chamber. Triplets and still higher multiple births may arise in the same way. In these cases the twins may be more or less closely united. Such mono-amniotic twinning is rare and only about 148 cases have been reported. The intra-uterine death rate is very high, mostly from entanglement of the cords.

The degree of resemblance between one-egg twins depends, in part at least, on the amount of cellular differentiation that has taken place before twinning starts. By the time the primitive streak forms the right and left sidedness of the germ disc is fixed and one embryo may get more and the other less of the right side material. The fact that Siamese twins, which are of the late forming class, are usually slightly different is explained in this way. One difficulty, however, in relating the degree of resemblance to the time of onset of twinning lies in the fact that the pattern of the membranes at birth may not be an accurate index of the stage at which the differentiation of the two embryos began to diverge.

The question has often been raised whether examination of the placenta and membranes gives reliable

information regarding the type of twinning in view of the possibility of deceptive fusion of the membranes, and even the conversion of two chorionic or amniotic cavities into one sac by disappearance of the membranous wall between them. Two placentas can certainly fuse into a single mass, and the adjacent chorionic walls of double ovum twins may blend into one layer and thin out so much as to suggest that only amnion is present. Hence microscopic examination of the membranous wall is necessary before the absence of chorion can be safely accepted. Present evidence indicates however that this is very rare in humans though it is a regular occurrence in the marmoset.

It follows that the placenta and membranes if carefully studied and the chorio-amniotic walls examined microscopically when necessary will generally yield a correct impression of the type of twinning.

This paper is profusely illustrated by rare examples of twin embryos mostly from the Carnegie collection.

F. J. Browne

187. **Social Class Selection and Class Differences in Relation to Stillbirths and Infant Deaths.**

By R. ILLSLEY. *Brit. med. J.*, **2**, 1520–1524. Dec. 24, 1955. 4 figs. 16 refs.

In the course of this socio-medical investigation, all married primiparae resident and delivered in the City of Aberdeen between July, 1950 and December, 1954 were studied. There were 4,344 such cases and in 3,911 of these detailed medical and social data were available.

In assessing the effect of environment on stillbirth and infant deaths, both the social class of the husband and that of the wife's father during her school years were taken into account.

The investigation shows that women who rise in social status at marriage tend to be of superior intelligence, education and occupational skill. They also tend to be tall, to be in good health and to have low prematurity and obstetric death rates. Such women tend not only to be superior in all respects to the remainder of the class of their upbringing but also to those brought up in the higher class whom they replace. On the other hand women whose social status falls at marriage appear to be inferior in all these characteristics and to have higher prematurity and obstetric death rates.

The author points out that such selective interchange between classes at marriage tends to accentuate class differences and that this explains in part, the continuing disparity between the mortality rates of the Registrar-General's social classes in spite of improved social and economic conditions in recent years. As these classes are changing in composition and size, and as movement between them is highly selective, comparison of class mortality rates at different periods of time may be misleading.

R. W. Grayburn

188. **Resuscitation of the Newborn Infant.**

By R. M. TOVELL, W. K. BANNISTER and D. M. LITTLE. *J. Amer. med. Ass.*, **159**, 1337–1338. Dec. 3, 1955.

This discussion is concerned with the chemical phenomenon of asphyxia neonatorum, the action of analeptic drugs, and antidotes administered to the mother during labour. The primary chemical change is extreme reduction in oxygen content, with secondary changes in lactic acid content, pH, and carbon dioxide tension. The transport of oxygen to the depressed cells of the respiratory centre is the real object of resuscitation, but cardiac activity is also depressed in hypoxia and the importance of the latter is reflected in the character and rate of the heartbeat which is the best index for evaluating the progress of an asphyxiated baby. The use of carbon dioxide in concentrations of 3 to 7 per cent as previously used is ineffective and may well be dangerous.

The dose of an analeptic drug (Nikethamide, alphalobeline, etc.) that produces effective stimulation of the respiratory centre is so close to the convulsant dose that there is little margin of safety, and their use should be discontinued. Nalorphine has a specific action towards improvement of respiratory and circulatory function only after the administration of morphine, meperidine or methedone. When given to subjects who are not depressed by a narcotic drug it may act like morphine and depress respiration. When respiratory depression is due to a barbiturate administration of nalorphine may produce a convulsion. The authors conclude that the most important factor is the skill and judgment of the resuscitator in establishing an airway and the administration of oxygen.

D. W. James

189. **Prematurity, The Obstetrician's Responsibility.**

By R. D. MACBETH. *Med. J. Aust.*, **2**, 724–727. Oct. 29, 1955. 1 fig. 1 table. 11 refs.

It should be the obstetrician's aim to find ways whereby the incidence of prematurity may be reduced and babies delivered safely and near term, ready for extra-uterine life. Approximately 60 per cent of foetal mortality is associated with prematurity, and this is the greatest cause of foetal loss. In this study the records of all those premature babies born alive at The Women's Hospital (Crown Street), Sydney in the year 1951–1952 have been examined. The total was 394, giving an incidence of 7·1 per cent out of a total of 5,552 live births. The neonatal mortality rate among mature infants at the hospital was 0·4 per cent. Of the 394 premature babies 10·6 per cent died in the neonatal period.

In 28 per cent there was no known cause for the premature birth. Pre-eclamptic toxaemia caused 23 per cent, hypertensive toxaemia 10 per cent, multiple pregnancy 9 per cent, placenta praevia 8 per cent and accidental ante-partum haemorrhage 5 per cent.

Antenatal care of the highest standard almost eliminates eclampsia and greatly reduces the incidence of pre-eclampsia. By a graph the author shows how the premature neonatal death rate at The Women's Hospital (Crown Street) fell concurrently with the fall in the incidence of eclampsia during the years 1942–1952. For the conduct of premature labour the author stresses the advantages to the baby of minimal maternal sedation, pudendal block, episiotomy, and at times a very careful

forceps delivery. Breech delivery is hazardous. The baby should get all the cord blood possible by tying the cord late. The nursing of the premature baby requires not only great skill, but constant vigilance day and night.

S. Devenish Meares

190. **Haemolytic Disease of the Newborn as a Family Problem.**

By W. WALKER and S. MURRAY. *Brit. med. J.*, **1**, 187–193. Jan. 28, 1956. 20 refs.

The histories of 1,033 immunized Rh-negative mothers, to whom were born 1,336 babies with haemolytic disease in Northumberland and Durham during the years 1947–55, are studied.

The object of the investigation was to ascertain whether or not there was any relationship between previous history and the severity of disease in later infants.

The following conclusions were reached:

(1) When immunization had been caused by an Rh-positive blood transfusion, the severity of disease in the infant was just the same as in cases where immunization had been caused by previous pregnancy.

(2) When no previous baby had been affected, 10 per cent of the babies might be expected to be stillborn, 50 per cent would be likely to require treatment and 40 per cent would not require treatment.

(3) In succeeding pregnancies there is a trend towards more severe disease but the authors show that this trend is not uniform in all cases.

(4) Other workers have demonstrated clear-cut family patterns but this investigation failed to show these and the authors believe that they are rare, but they found that the form and severity of disease in the immediately preceding pregnancy is of great prognostic value. For example, a stillbirth rate of no more than 2 per cent might be expected when a previous infant was only mildly affected and required no treatment. Of those born alive under these same circumstances, 60 per cent would survive without treatment. On the other hand, if the previous baby had been stillborn because of haemolytic disease, there would be an 80 per cent chance of the next one being stillborn if labour were allowed to commence spontaneously. These babies born alive would be severely affected.

(5) A previous history of kernicterus carries no worse prognosis than the previous occurrence of an affected baby requiring treatment.

(6) The interspersing of the family with normal Rh negative babies does not alter the prognosis for further pregnancies, which must be based on the severity of disease in the last Rh-positive infant.

(7) Immunization from an early pregnancy was only slightly more serious than immunization from a later pregnancy.

(8) There is no relationship between severity of disease and spacing of pregnancies.

The authors confirm that the risk of immunization to the Rhesus factor is greater when the father is compatible with the mother within the ABO groups. They could find no relationship between the ABO groups of mother, father or child and severity of disease, once immunization had occurred.

They also show that there is an increased risk of stillbirth when the pregnancy of an immunized mother is complicated by pre-eclampsia though it is uncertain which is cause and which is effect.

Finally, the investigation suggests that abortions may be caused by haemolytic disease, and, if so, their significance in relation to subsequent babies is similar to that of stillbirth due to haemolytic disease.

R. W. Grayburn

191. **A Rare Case of Multiple Intrauterine Foetal Fractures, Caused by Osteogenesis Imperfecta, of Vrölik's Type.** (Su di un raro caso di fratture fetali multipe endouterine per osteogenesi imperfetta tipo Vrölik.)

By M. MARCHESONI and A. HELFER. *Ann. Ostet. Ginec.*, **77**, 585–594. June 1955. 7 figs. 27 refs.

A report is given of the case of a 30-year-old woman who had had one normal male infant. Her second pregnancy was normal. A female infant was born in good condition but deformity of the lower limbs was noted. X-rays revealed fractures of both femurs, of the left humerus and of two ribs. In some of the fractures callus formation was evident. The infant was breast fed and progressed well. At 68 days there were fractures of both humeri. In view of the infant's excellent general progress it was felt that the outlook for the future was good. A detailed study of the family pedigree revealed no other cases in four generations. *Josephine Barnes*

192. **Congenital Malformations: Analysis of the 1953 Ohio Records.**

By C. H. HENDRICKS. *Obstet. Gynec.*, **6**, 592–598. Dec. 1955. 2 figs. 8 tables, 7 refs.

In 1953, there were 1,560 live born congenitally malformed infants among 210,727 births in Ohio, an incidence of 0·74 per cent. The author notes that Murphy has calculated that malformations are seen 5·5 times more often among stillbirths than among live born infants. The foetal abnormality rate was found to be very high (22·5 per thousand) when the mothers were under 15 years old and when they were over 44 (26 per thousand). In the maternal age group 20–35, the foetal abnormality rate was between 6·4 and 7·8 per thousand. There was no evidence that malformation was more common amongst primigravidae or among white parents.

The malformation rate was found to be more common for males than females, being 7·8 and 6·7 per 1,000 respectively. Twinning increases the hazard of producing a malformed child. The risk of giving birth to at least one deformed twin is 2½ times that for a single foetus.

The percentage of prematurity among deformed infants, judged both by weight and gestational age, was over 2½ times that found among all 1953 Ohio births.

J. G. Dumoulin

GYNAECOLOGY

193. **Gynaecological Disorders in the Adolescent.** (Les troubles génitaux chez l'adolescente.)

By J. BARNES. *Gynée. prat.*, **6**, 305–313. 1955.

This article presents a summary of British treatment of the commoner gynaecological disorders of adolescence. Miss Barnes points out that organic lesions are rare at this epoch but that careful search must be made for them. She advocates the treatment of functional amenorrhoea, both primary and secondary by a modification of the Hamblen regime. If sufficiently severe to require such therapy, puberty menorrhagia may be treated with haemostatic oestrogens, followed by the production of artificial cycles for some six months. The administration of small doses of oestrogen throughout the cycle except the actual days of menstruation is a satisfactory treatment of dysmenorrhoea. Miss Barnes suggests that this therapy is effective, not on account of suppression of ovulation but by a local effect on the uterus.

Except when associated with an ovarian tumour, precocious puberty is better left untreated. In general, vaginal discharge in the young girl raises the same problems as in the adult and is to be treated along the same lines.

[Written for a French journal, this article will no doubt be studied with great interest on the Continent where the liberal use of oestrogens in functional disorders of menstruation is not in vogue.]

Geoffrey Dixon

194. **A Form of Intersexuality.**

By L. R. Broster. *Brit. med. J.*, **1**, 149–151. Jan. 21, 1956. 2 figs. 3 refs.

When the sex of an infant is indeterminate the diagnosis, in general, lies between (1) the adrenal pseudohermaphrodite, (2) the true hermaphrodite, (3) the intersex, and (4) the cryptorchid.

Each type has hypospadias and an enlarged phallus. Two extreme forms of hypospadias can be recognized. One is predominantly female with an open urethral groove and enlarged clitoris, and the other predominantly male with a partly fused urethral groove and a small flexed penis with prepuce. The adrenal pseudohermaphrodite conforms to the former type. The author reviews three cases belonging to the latter. In the first case a preliminary diagnosis of adrenal pseudohermaphroditism was made but it was found that the ketosteroid excretion was normal and not raised as should have been expected. Some form of intersex was then suspected but normal adrenals, a uterus and ovaries were found. Skin biopsy showed that the chromosome pattern (Barr) was female. The other two cases were similar.

The author considers it unwise to speculate on the mode of origin of the abnormalities reported, but emphasizes that it is not primarily adrenal. Only their future development will show whether it is only a local manifestation or part of a more general somatic change.

R. W. Grayburn

195. **A Clinical Review of 550 Cases of Prolapse of the Uterus.**

By R. G. Krishnan. *J. Obstet. Gynaec. India*, **6**, 155–161. Dec. 1955.

This paper was read at the Eighth All-India Congress of Obstetrics and Gynaecology, and is a review of the author's personal cases. Prolapse is stated to be the commonest gynaecological condition in the State in which the author works, having an incidence of almost 40 per cent of all cases seen. This he attributes partly to the local custom of keeping a woman in bed for 56 days after delivery. Another factor is the straining during the first stage of labour, which is encouraged by district midwives. Prolapse occurs more often in younger age groups than is the case in this country, over 70 per cent occurring between 20 and 40 years of age, with a maximum incidence in the 20–30 age group. Most of the women had by then borne between 6 and 10 children.

As regards symptoms, it seems that stress incontinence is much rarer than in the Western world, and in this series, occurred in only 7 of the 550 cases. Other urinary symptoms were, however, common.

Carcinoma of the cervix accompanying prolapse seems more common than is usual in this country. [The incidence cannot be gauged, as the number given in the tables contradicts the text.]

Operative treatment was much the same as is advocated in Britain, except that a vaginal hysterectomy was more commonly practised, and was done in all women who did not want any more children, or who had reached the menopause. Twenty women were sterilized through the utero-vesical pouch. There were 3 deaths, the causes of which are not clear, as the abdomen was opened in 27 cases for various reasons unrelated to the prolapse.

J. McKiddie

FUNCTIONAL DISORDERS

196. **Functional Haemorrhage.** (Contribution à l'étude des hémorragies fonctionnelles.)

By G. Duperroy. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 475–482. 1955. 28 refs.

This is a thorough histopathological study of the myometrium and endometrium of 18 uteri removed for "functional" haemorrhages during the reproductive years, for which no local or general cause was found, and which persisted after several curettages and after conservative treatment. Twelve uteri from patients with normal menstruation, and 8 from post-menopausal patients were also studied.

Clinical and histological analysis shows a significant correlation between the pathological haemorrhages and *either* the sclerosis of types II and III of the basal endometrial spiral arteries, *or* the disappearance of those arteries. A similar conclusion has been drawn from a previous study of menstrual disorders in myomatous uteri.

In the light of Markee's work on the mechanism of normal menstrual haemostasis, the author suggests that the endometrial arterial lesions are an "organic" explanation for many abnormal haemorrhages that have so far been considered to be "functional".

From the Author's Summary

197. **The Biological Action of Methylandrostenediol.** (Contributo alla conoscenza dell'azione biologica del metilandrostenediolo.)

By G. Tronconi. *Ann. Ostet. Ginec.*, **77**, 657–680. July 1955. 18 figs. 119 refs.

The chemical formula and physical properties of methylandrostenediol are described. Its biological properties were tested in experimental animals with the following results.

Methylandrostenediol has a slight but definite masculinizing effect, as tested by weight gain in the seminal vesicles and prostate of the castrated rat. The effect was one-tenth of that of testosterone and one-twelfth of that of methyl testosterone. Methylandrostenediol has some effect in causing spermatogenesis. In castrated female animals, it acts as a progestogen, the effect being one-third of that of progesterone. It has an anti-oestrogenic effect when tested on the vaginal epithelium of castrated rats. It has a pituitary inhibiting effect and was found to suppress ovulation in rats. It has a pluriglandular effect, causing atrophy of the suprarenal cortex in rats. In pregnant rats, death of the foetus resulted; there was pseudohermaphroditism in female foetuses and arrest of development, perhaps through the effect on the placental metabolism. It was found to have a definite effect in producing protein anabolism. An antineoplastic effect was demonstrated in experimental tumours.

In clinical practice, methylandrostenediol may be used for its protein anabolic effect in cases of loss of weight and infantilism. It is also useful in cases of osteoporosis. In malignant disease it causes subjective improvement and regression of metastases; it is especially useful in metastases from mammary carcinoma. In gynaecology it has been successfully used in spasmodic dysmenorrhoea and premenstrual tension.

Further experimental observations on rats showed that methylandrostenediol causes wrinkling and vacuolation of the liver cells. Marked changes were seen in the spleen, inhibition of the follicular system and increase in haemosiderin pigments. In the kidney, hypertrophy of the tubules occurred. Large doses cause shrinking in the adrenal cortex and inhibition of thyroid function. In the ovary, large doses caused involution of the follicular system, with thecal hyperplasia. In the uterus, a dose of 100 mg. had an oestrogenic effect, while a dose of 500 mg. produced a progestogenic effect. Similar effects were seen in the vagina of the castrated rat.

In clinical use it not only had an effect on protein metabolism but it caused retention of sodium, potassium, phosphorus and calcium. Basal metabolic rate was lowered but haemoglobin levels rose. There was also a rise in red cells. Withdrawal bleeding from the uterus sometimes occurred on stopping treatment.

It is considered that methylandrostenediol is to be preferred to testosterone when used for its metabolic effects, since the action on the genital tract is much less marked.

Josephine Barnes

198. **Cervical Aspects in Sterility and Infertility.**
By W. Steinberg. *Fertil. Steril.*, **6**, 169–177. Mar.–Apr. 1955.

Because the lining of the uterine cavity and that of the cervix have a common embryological origin one would expect that the cyclic changes seen in the one would occur in the other. As regards the cell lining this has been denied though there is no question that the cervical secretion undergoes not only cyclic variations due to oestrogens, but alters in its pH and viscosity. Papanicolaou was the first to observe in 1945 the fern phenomenon peculiar to ovulation, but it was Da Paz who observed that the fern crystals disappeared after the 22nd day of the cycle due to the effect of progesterone if ovulation is normal. The cervix is the key to the problem of infertility in over 30 per cent of all infertile patients. This can often be proved by the finding of less than 10 actively mobile sperms per high power field when doing the Huhner test though of course such showing must be confirmed by expert sperm analysis as well. If no living sperms are visible in the cervical sample it may be that either they have been unable to penetrate the cervical mucus, or that they have been devitalized thereby. Today the spermatologist should not concentrate so much upon the immobility or oscillation of the sperm cell, as upon its ability to travel from one side of the high power cover slip to the other. Dr. Steinberg is strongly in favour of the spinnbar test of Clift being done around the time of ovulation and agrees that the stretchability of the mucus should not be less than 2½–3 inches. In those cases where immobility of the spermatozoa in the cervical mucus was a feature, he thinks this phenomenon is due to saccharopenia. In this connexion it is perhaps worth mentioning that viability and transit motility of the spermatozoa both *in vitro* and in the cervix has been found to be greatly increased by giving the husband at the time of his wife's ovulating period 5 mg. of Dexedrine between 10 and 11 a.m. for 2 or 3 days.

V. B. Green-Armytage

199. **Testicular Biopsy: Which Infertile Patients are Benefited?**
By S. Paine and R. F. Skeels. *Fertil. Steril.*, **6**, 43–50. Jan.–Feb. 1955.

In the past much discomfort, expense and apprehension have been occasioned by useless and unnecessary biopsies. The authors after long experience are of the opinion that the only real indication for testicular biopsy is the azoospermic patient with normal sized testes in whom there is doubt as to the presence of an obstructing lesion in the vas. They are of the opinion that conditions of oligospermia do not demand this test, for the specialist can make his diagnosis and prognosis by other clinical methods, and most particularly by the size and feel of the testes.

V. B. Green-Armytage

200. **The Effects of Cortisone on the Infertile Male.**
By L. Michelson, S. Roland and P. Koets. *Fertil. Steril.*, **6**, 493–505. Nov.–Dec. 1955.

It was hoped that cortisone might be of assistance in cases of deficient spermatogenesis. Many patients were submitted to treatment by the authors but after much experience it was shown to be of no value whatever. Indeed, as in the case of testosterone, sperm counts were found to become depressed while on cortisone treatment, and did not rise beyond their original levels

until after it was discontinued, nor was there any increase in semen volume or sperm motility.

V. B. Green-Armytage

201. **Cortisone in Sterility.**

By W. FINEGOLD. *Fertil. Steril.*, **7**, 28–30. Jan.–Feb. 1956.

One hundred couples were selected for trial because no cause for infertility could be found in either party; 91 were cases of primary sterility and 9 of secondary sterility. An average dose of 25 mg. of cortisone was given once, or even twice a day, and the patient's diet was restricted to a low salt and carbohydrate content for 4 months. The patient was supervised every 2 weeks to ensure that she did not develop oedema, hirsutism or gain in weight. Of these patients 23 became pregnant, and this after a very short interval, which would suggest that the cortisone had some metabolic effect, possibly through the thyroid, or perhaps through increased libido and the psyche. Anyhow it would appear that such patients need careful watching during the administration of this expensive hormone.

V. B. Green-Armytage

202. **Roentgen Therapy in Anovulation and Sterility.**

By T. M. FULLENLOVE, J. O. HAMAN and A. J. WILLIAMS. *Fertil. Steril.*, **7**, 18–27. Jan.–Feb. 1956.

This is a controversial and interesting paper giving the authoritative "pros" and "cons" for this line of treatment. Those against it are influenced by the geneticists who oppose X-rays on the grounds of work done on the drosophila and rabbit, and who prophesy dangers to the human race in the third and fourth generations. On the other hand those in favour of it do not believe that the genetic objections are valid because a very small number of child-bearing women in relation to the total are treated, and because the dosage is so small and well regulated. Moreover, they have been able to show that the second and third generation of children from an originally irradiated mother are normal. Kaplan of New York is the outstanding proponent of radiation and states that in his own cases no abnormality has been found for 3 generations in the offspring of irradiated women. It would seem from the individual reports of many gynaecologists and radiologists that proper application of X-rays to carefully selected patients suffering from ovarian dysfunction is beneficial. Out of 104 patients who were treated for anovulation and infertility it is shown that 46 became pregnant and 22 began to ovulate again. For these reasons the authors are not prepared to accept that a 1,000 years from now that there will be a great increase in hereditary mutations.

V. B. Green-Armytage

203. **Irradiation and Ovulation. X-ray Treatment of Ovaries and Pituitary in Anovulatory Cycles.**

By E. G. INGALLS, P. N. LARSON and M. S. ROTHNEM. *Obstet. Gynec.*, **6**, 610–614. Dec. 1955. 8 tables. 8 refs.

The authors state "If one can philosophically justify what may be a genetically perilous pursuit and if one is willing to employ empirically a weapon of known value despite a lack of physiological backing, then X-ray treatment to the ovaries and pituitary belongs in the therapeutic armamentaria of gynaecologists".

During a 12-year period the authors have irradiated the ovaries and pituitary in 106 patients. The indications were sterility in 68 cases, amenorrhoea in 20 cases, irregular menses in 15 cases, menometrorrhagia in 2 cases and acne in 1 case.

Of the 60 infertile cases followed up, 25 conceived within 1 year and in all 37 (61·8 per cent) conceived. The number of faulty conceptions did not appear to be higher than in a routine pregnancy series. Of 60 patients in the series adequately followed, 80 per cent were proved to have an ovulatory endometrium after treatment.

J. G. Dumoulin

INFECTIONS OF THE REPRODUCTIVE ORGANS

204. **Pelvic Tuberculosis: Its Relationship to Sterility, Present and Future.**

By D. W. DE CARLE. *Fertil. Steril.*, **6**, 534–539. Nov.–Dec. 1955.

The author discusses the devastating effect of tuberculosis from the point of view of infertility, and shows that the process of healing in the tubes occurs by fibrous infiltration into their walls. This interferes with the normal function of these organs, namely tubal peristalsis. Moreover, the process results in multiple strictures, both inside and outside the tubes, which cause distortion and obliteration of the lumen. He does not know of any accredited case of pregnancy that has occurred after a definite diagnosis of pelvic tuberculosis, and he calls attention to the fact that pelvic surgery in the presence of this disease has an actual mortality of approximately 20 per cent. He advocates streptomycin and PAS treatment therefore as the alternative, and does not think that fertility in such cases can be expected unless medical treatment is collateral with early diagnosis.

V. B. Green-Armytage

205. **Growth and Life Cycle of *Trichomonas vaginalis* and the Mechanism of Recurrence of *Trichomonas vaginalis* Vaginitis.**

By A. SHINOZUKA. *J. jap. Obstet. Gynec. Soc.* (English edition), **2**, No. 1. Jan. 1955. 10 plates. 13 refs.

The author has studied the morphology of *Trichomonas vaginalis* in culture media under variations of temperature and pH. He also records the effects of trichomonacidal agents. In an unfavourable environment (infusion of a trichomonacidal agent, abnormal temperatures and pH changes) the trichomonas becomes a ball-shaped organism or "cyst". The "cyst" is capable of becoming an active flagellate when replaced in a favourable environment. The survival of the organism in this "cyst" form could explain the recurrence of trichomonas vaginitis after clinical and bacteriological cures.

The author has never found the trichomonas in the male but believes that it lurks in the female bladder, Skene's tubules and in Bartholin's glands.

In the treatment of 600 cases the author noticed that the patients with cervical erosions were most refractory. This led to a study of the tissue pathology of cervical

erosions in cases of trichomonas vaginitis. In the biopsy specimens the author found a homogeneous round substance staining red with eosin in amongst the layers of epithelial cells. This has been named a "trichomonad corpuscle". In 28 cases where this was found *Trichomonas vaginalis* was found in 26 cases. The "trichomonad corpuscles" are described as nearly spherical, variable in size from 3–15 microns in diameter and are not unlike Russell's bodies. The author regards them as a live trichomonas organism adapting itself to the environment of the tissue in which it is embedded. No attempt is made to correlate the "cyst" discovered in the experimental work and the "trichomonad corpuscle" found in the biopsy specimens. The author reports that further studies are in progress.

J. R. E. James

206. **Inflammation of the Pouch of Douglas due to Foreign Body.** (Syndrome de Douglassite par corps étranger.)

By P. Loy. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 460–467. 1955. 4 figs.

In a 33-year-old woman who had suffered for 10 years from congestive Douglasitis with chronic adnexitis a pelvic X-ray showed a rounded opacity in front of the 5th sacral vertebra, which was interpreted as the shadow of a steel ball. At hystero-adnexectomy the foreign body could not be found. In a post-operative X-ray the opaque shadow had fragmented into small particles; it was a ball of lipiodol which had remained since a hysterosalpingogram eight years previously. Recovery followed with absorption of the lipiodol.

From the Author's Summary

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

207. **Postgranulomatous Carcinoma of the Vulva.**

By S. L. Saltzstein, J. D. Woodruff and E. R. Novak. *Obstet. Gynec.*, **7**, 80–90. Jan. 1956. 34 refs.

During the period 1932–53 58 cases of carcinoma of the vulva were admitted to The Johns Hopkins Hospital; but in 8 cases the diagnosis was inconclusive or treatment had been given elsewhere, leaving 50 cases for review. Thirteen of these patients had a history of granuloma, 5 of lymphogranuloma venereum, 3 of positive smears for Donovan bodies, 2 of granuloma inguinale, and 3 of condylomata acuminata. Twelve of the 13 cases had either positive serology for syphilis or a history of "needle treatments". The remaining group of 37 had no evidence of pre-existing granulomatous lesions.

The 2 groups were compared. They showed an age discrepancy. The average age in the granulomatous group was 42 and in the other group 60. The presenting symptoms in half the first group were bleeding, ulceration, discomfort or a palpable mass, the remainder complaining of the more usual symptom—pruritus.

In the carcinomas preceded by granulomatous lesions there was a high percentage of histologically undifferentiated tumours, whereas the predominant type in the general group was the spinal cell. Lymphatic gland involvement in the granulomatous group was rare possibly because the pre-existing disease sealed off the lymphatic drainage often with the development of elephantiasis.

J. G. Dumoulin

208. **Vaginal Cytology in the Early Diagnosis of Carcinoma of the Cervix.** (La cytologie vaginale dans le diagnostic précoce du cancer du col de l'utérus.)

By L. Baciallı. *Gynéc. prat.*, **6**, 316–321. 1955.

This is the first report of the routine use of the Papanicolaou smear to come from Italy.

The investigation was carried out on 5,258 patients between 1946–1954. Four hundred and forty-three carcinomas of the cervix were detected. After a preliminary discourse on the causes of error in interpretation, the author has classified his results as follows:

Group A (false negatives), 35 cases. Cytology negative. Biopsy positive.

Group B, 375 cases. Cytology and biopsy positive.

Group C, 13 cases. Cytology positive. Biopsy performed on this account alone. All positive.

Group D, 20 cases. Cytology positive. Biopsy negative in first instance, but later positive.

Group E (false positives), 55 cases. Cytology positive. Biopsy negative. The author comments that further follow-up may show the cytological findings to be correct.

Group F, 62 cases. Cytology inconclusive in the first instance. Biopsy negative. These results were mostly obtained during the author's early experience of the technique.

Group G, 2,704 cases. Cytology and biopsy negative.

Group H, 1,995 cases. Cytology negative. Biopsy not undertaken.

The author stresses the cases in Groups C and D as confirming the value of vaginal cytology as a routine investigation. He claims a percentage of error of 1·83. This figure is calculated from the total cases and not from the total of carcinomata detected.

Geoffrey Dixon

209. **The Treatment of Cystic Ovaries with Micronized Vitaminized Stilbestrol. A Twenty Year Study.**

By K. J. Karnaky. *West. J. Surg. Obstet. Gynec.*, **64**, 39–44. Jan. 1956. 4 refs.

The author is concerned that many ovaries removed at laparotomy might be salvaged in spite of the fact that they contain follicular or corpus luteum cysts with or without haemorrhages. He briefly discusses the endocrine control of the ovaries and points out that synthetic oestrogens, particularly stilboestrol, will produce atrophy of the normal ovary and in many cases, cause regression of the polycystic ovary; follicular cysts and corpus luteum cysts are also amenable to treatment.

The patient is given 21 one-milligram tablets of micronized vitaminized stilboestrol (micronized meaning that the crystals are from $\frac{1}{4}$ to 1 micron in diameter and thus able to pass between the cells of the gastro-intestinal tract directly into the blood stream; vitaminized means that vitamin B complex and C plus trace elements are added). One tablet is taken at night and the dose increased

by one tablet nightly until 6 tablets are being taken; she then takes one 25 mg. tablet at night and increases the dosage to four 25 mg. tablets; 4 tablets are then taken nightly for 3–4 weeks or until the cysts disappear. The patient is examined every 10 days to assess the progress of treatment. At the conclusion of treatment it is important to avoid withdrawal bleeding and the dosage of stilboestrol must be gradually reduced. Three 25 mg. tablets are taken one night, 2 the next night, 1 for one night; and then 0·75 mg.; 0·50 mg.; 0·25 mg. for one night and then she stops. If there is any excessive bleeding the patient takes one 1 mg. tablet every 15 minutes until the bleeding stops; bed rest and Ergotrate tablets every 2 hours aid in checking this bleeding.

The addition of vitamins to the stilboestrol is considered important as this aids the metabolism of the synthetic oestrogen and stops side effects such as nausea and vomiting.

Altogether 224 patients were treated, 25 receiving no relief. These patients were operated upon and various truly pathological lesions discovered.

D. C. A. Bevis

210. **A Histochemical Study of Ovarian Cystomata.** (Studio istochimico dei cistomi ovarici.)

By A. GASTALDI. *Ann. Ostet. Ginec.*, **77**, 551–558. June 1955. 4 figs. 19 refs.

Detailed histochemical studies on serous cystadenomata of the ovary and ovarian pseudomucinous cystadenomata are described with reference to the probable sites of origin of these tumours.

The author concludes that serous cystadenomata probably arise from the germinal epithelium of the ovary. He believes that serous cystadenomata rise from rests of Müllerian epithelium in the ovary.

Josephine Barnes

211. **The Management of Bilateral Polycystic Ovaries.**

By I. F. STEIN, Snr. *Fertil. Steril.*, **6**, 189–205. May–June 1955.

All of us from time to time have met the young woman who presents the problem of infertility accompanied by amenorrhoea and mild hirsutism; in others the periods are too frequent and may be accompanied by acne and pelvic pain. In the majority of these two types the uterus is obviously hypoplasic and the breasts are underdeveloped. Moreover, by all tests they are all non-ovulatory. In 9 out of 10 cases these patients have palpable ovaries, which can be seen by culdoscopy. Often the cervical mucus is scanty and has a spinnbar of but half an inch. Occasionally they have the typical male escutcheon and should endometrial biopsy be done the predominant type is a low degree of proliferation. Dr. Stein uses pneumograms to investigate these cases and is a confirmed believer in the value of horizontal wedge resection of each ovary. He reports that in 32 out of 45 patients a regular menstrual cycle was re-established and 14 pregnancies occurred; and in another series where 36 surgeons reported upon 568 patients so operated upon, he records that 75 per cent menstruated regularly afterwards and that 37 per cent became pregnant giving birth to 215 infants. In his own experience medical therapy or hormones were of no value. After wedge resection normal menstruation occurred within a few months in 95 per cent of patients. He is of the opinion that secondary amenorrhoea, apart from obvious causes, is definitely associated with the polycystic ovary and that the syndrome of symptoms mentioned above is a recognizable feature. He considers that the pneumograph is an important aid to diagnosis and the name given to the syndrome described should be that of Stein-Leventhal.

V. B. Green-Armytage

212. **Classification of Ovarian Tumours.** (Le classificazione dei tumori ovarici.)

By F. FERRARIS and G. BONGIOVANNI. *Ann. Ostet. Ginec.*, **77**, 705–723. July, 1955. 61 refs.

A critical review is given of the most important classifications of ovarian tumours.

The first is that of Vegas (1864), and a similar one was produced by Laskoski in 1867. Other nineteenth century authors include Waldeyer, 1870, Fernbach, 1867, Malassex and de Snety, 1882 and Pfannenstiel, 1895.

In the present century, attempts to classify ovarian tumours are quoted from Masson, 1923, Bell, 1931 and Barzilain, 1936. Later Müller, 1937 presented a simple classification while Schiller, 1939 produced one much more elaborate. Malcovati, 1948, classified ovarian tumours in seven main groups. Willis, 1948 produced eight groups. Natali, 1949 modified and simplified Malcovati's classification. In 1950, Von Numers described that of Spencer and Reel, modified from Schiller. A further contribution was that of Novak (1953).

The work of many other authors on the problems of the origin and classification of ovarian tumours is quoted, notably that of Meyer.

The authors conclude that ovarian tumours can best be divided into the following groups: functioning tumours, cancers, cysts, connective tissue tumours, teratomata and endometriomata.

[This is a difficult paper to abstract, especially as the authors do not give the complete references of the work they quote and many papers cited are omitted from the list of references. It is of academic interest in relation to the many attempts that have been made to solve the difficult task of classification of the tumours of the ovary.]

Josephine Barnes

213. **Two New Cases of "Démon-Meigs" Syndrome.** (Deux nouveaux cas de "syndrome de Démon-Meigs".)

By G. WINTGENS. *Bull. Soc. belg. Gynéc. Obstét.*, **25**, 432–438. 1955. 4 figs. 12 refs.

The author reports two cases of ovarian tumour with ascites and hydrothorax. He describes the problems of pathology and the divergent views about this syndrome, and points out that it is necessary to be familiar with it in order to treat it effectively.

From the Author's Summary

214. **Malignant Ovarian Tumours.**

By B. N. PURANDARE and G. N. PATWARDHAN. *J. Obstet. Gynaec. India*, **6**, 111–118. Dec. 1955.

This paper was read at the Eighth All-India Obstetric and Gynaecological Congress.

An analysis is made of the malignant ovarian tumours occurring in the K. E. M. Hospital, Parel, over a 12-year period. There was a total of 300 ovarian tumours, of which 69 were malignant, giving an incidence of 23 per cent. Five cases occurred between the ages of 16–20, and the greatest number occurred in the 31–35 age group. [The latter figure did not tally with that given by other speakers at the Congress.]

In all cases where ovarian malignancy is suspected, the routine investigations include a straight X-ray of the abdomen, a barium follow-through, an intravenous pyelogram, vaginal cytology, cystoscopy, and biochemical blood investigations.

The symptoms and signs are enumerated.

The authors mention the difficulty of comparing data owing to the lack of uniformity of the classification of ovarian neoplasms. They discuss the difficulty in cases where a unilateral ovarian tumour is removed, and is shown microscopically to be malignant, and the suggestion is made that in all cases the apparently healthy ovary may be bisected, and the cut surface inspected at the time of operation. If the disease is not widespread, they achieve better results with deep X-ray therapy combined with surgery, than with surgery alone. They mention the failure of the massive doses of male hormone which have been tried in inoperable cases, and think that bilateral oöphorectomy should be considered in all women over 45 years of age who have a pathological condition in the pelvis.

J. McKiddie

OPERATIONS

215. **Hysterosalpingography. Oily or Water-soluble Contrast Media?** (Hystérographies aux huiles iodées ou aux organo-iodés hydro-solubles.)

By J. MONTAGNON. *Gynéc. prat.*, **6**, 323–333. 1955. 30 figs.

The author has carried out hysterosalpingograms at an interval of a few days with both types of media on a series of cases.

As a result of this investigation he concludes that although difficulties of technique and interpretations are greater with the water soluble media, this is more than compensated by the more exact and detailed information obtained. The technical difficulties are such that the method is not suitable for beginners and apart from this there are indications (not specified in the article) for the use of oily media.

Geoffrey Dixon

216. **The Advantages and Limitations of the Interposition Operation.**

By D. W. DE CARLE. *West. J. Surg. Obstet. Gynec.*, **64**, 1–3. Jan. 1956. 8 refs.

Following a brief review of recent papers about the Watkins-Wertheim interposition operation, the author discusses the indications for it. It is suitable for cases with a pronounced but uncomplicated cystocele, or a well defined but moderate prolapse and a mild urinary incontinence. It must not be performed before the menopause, and the uterus must be freely mobile and healthy. It is better to employ some other technique in the presence of fibroids, although an atrophic organ may be used very successfully. From the results obtained in 29 personal cases, the author concludes that the operation gives excellent results in selected patients.

[This technique does not appear to offer any advantage over the usual type of colporrhaphy performed in this country.] *D. C. A. Bevis*

217. **Current Concepts of Ovarian Surgery.**

By R. H. BARTER and J. PARKS. *Obstet. Gynec.*, **7**, 62–69. Jan. 1956. 29 refs.

In patients with ovarian tumours the history is usually not of great significance. Malignant growths are often "silent". Acute pain suggests torsion of the pedicle of an ovarian tumour. Persistent pain is commonly a complaint in carcinoma of the ovary when there has been haemorrhage into the tumour. There is a higher incidence of ovarian carcinoma in some families. Cystic ovarian tumours of small size (less than 5 cm.) are usually physiological enlargements. Solid tumours are more likely to be malignant than cystic ones. Unnecessary ovarian surgery is frequently performed in hysterical women.

When surgery is indicated, the following principles are important:

(1) Adequate exposure. There is no place for aspiration of large tumours in order to remove the collapsed cyst through a small incision.

(2) Complete examination. Before exploring the pelvis the upper abdomen should be examined, including bowel, liver, gall bladder, kidneys and aortic nodes.

(3) The most conservative procedure possible should be done with benign lesions. All tumours removed should be examined carefully before the abdomen is closed.

(4) In the treatment of malignant lesions, the omentum should be removed with the ovaries and uterus.

(5) Routine removal of normal looking ovaries when doing a hysterectomy is not justifiable. If done, it may result in an increased incidence of osteoporosis, senile vaginitis, severe menopausal symptoms and coronary disease. *J. G. Dumoulin*

NOTICES

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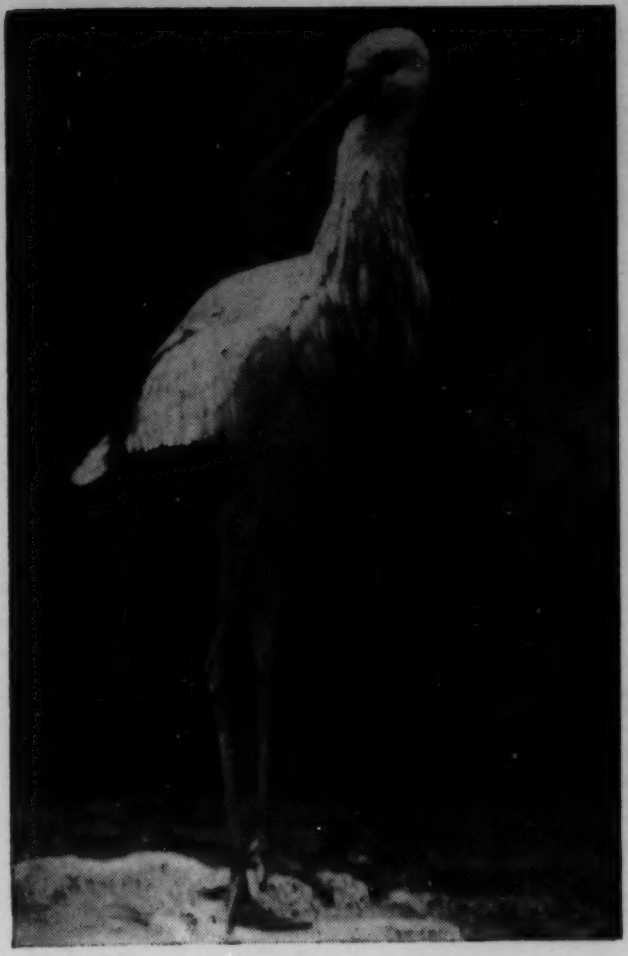

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